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EDITORIAL

THE DENTIST'S RESPONSIBILITY IN DIAGNOSIS AND TREATMENT OF CANCER*

EDWARD TELLER, in a recent article entitled "The Work of Many People" (Science **121**: 267, 1955), describes the development of the hydrogen bomb. It is a fascinating story competently told. Dr. Teller begins with a refugee from Soviet Russia who had a "wonderful sense for interesting problems." In 1928, six years before this refugee came to the United States, he had reported in the Academy of Sciences of the U.S.S.R. a paper published by two physicists, one English and one German. In this paper it was suggested that the apparently inexhaustible energy of the sun and other stars was derived from reactions between atomic nuclei occurring at exceedingly high temperatures, now commonly referred to as thermonuclear reactions.

After the lecture this Russian scientist was approached by a high Soviet official who asked whether such nuclear reactions occurring in the sun could be produced here on earth and utilized. The scientist replied that the practical difficulties were too great, but he did not forget the suggestion. Years later the atomic bomb furnished conditions which made development of the hydrogen bomb possible. In this development the "idea man," the engineer, and the statesman all play the indispensable roles.

Cancer studies also are the work of many persons at many levels. To the individual, cancer is a catastrophe of the order of magnitude that the hydrogen bomb is to society. The cancer problem is being attacked by "idea men" (the research workers), by the pathologists who are responsible for the definitive diagnosis, and by clinicians who must care for the patient here and now. Cancer is a biologic problem more complex than the release of energy by the sun, since a cell is far more complicated than a hydrogen atom. No one familiar with the cancer problem can believe that our present methods of diagnosis and treatment will not soon be superseded by far more effective measures. Modern radiology and surgery, highly developed though they are,

*When this publication was in the planning stages, it was learned that the July-August issue of *CA: Bulletin of Cancer Progress* was to be devoted exclusively to mouth cancer. Since the guest editor for this issue of that journal is on the editorial board of ORAL SURGERY, ORAL MEDICINE AND ORAL PATHOLOGY, it seems appropriate that his editorial and the oral cancer issue of *CA: Bulletin of Cancer Progress* appear simultaneously.

in essence only destroy the diseased area by burning it out or by cutting it out. They succeed only when the last cancer cell is destroyed or removed and, with few exceptions, only if the primary growth is adequately treated before metastases occur. Diagnosis, at present, consists usually of discovering a full-grown lump, mass, or ulcer which by biopsy and microscopic examination is identified as a cancerous growth. Exfoliative cytology is a long step forward, and someday—soon, we hope—we will have other methods of identification of early changes long before a mass is clinically detectable. Eventually we will prevent cancer rather than attempt to destroy it after it develops.

We dentists are practical people. We deal with the patient at the present moment. What is the problem? What is our responsibility? What can and should we do about it? We are in the position of the politician who must decide today and let history determine whether or not the decision was statesmanlike.

First, the problem. Just what is cancer? Most of us have gained a strong impression that it is a dreadful disease leading more or less inevitably to a horrible death. Furthermore, it is associated in our minds with mutilation and deformity which may make its victims social outcasts. We have all heard that cancer is now the second most important cause of death. All of us fear cancer with some of the Old Testament loathing of disfiguring disease. The American Cancer Society's campaign to emphasize the curability of cancer has been designed to overcome this deep fear. We, as dentists, as experts in the diseases of the mouth, can do much to bring this fear out into the light and to allay it. Most of our patients over 40 years of age have some degree of cancerophobia. After completing a thorough visual and digital examination of the soft tissues of the mouth, pharynx, lips and neck, it is sound psychology to say: "I find no evidence of cancer." You may be astonished at how many of your most intelligent patients will say: "Thank you, Doctor; I was a little worried about that." Then it is just as well to add: "I see no conditions that are likely to become cancerous," for patients start worrying again after they leave the office. A careful, complete examination of the entire mouth cavity and associated parts is our professional responsibility. If we, as dentists, do not function as stomatologists, assuming responsibility for diagnosis of all the diseases of the mouth, as the ophthalmologist does for the diseases of the eye, we may find ourselves caught between the medical profession above and the hygienist and laboratory technician below. We must, by the competence of our professional knowledge and performance, justify our long and expensive education and our preferred and privileged place in society. The dentist's first responsibility in the diagnosis and treatment of cancer is a complete and thorough examination of the oral region at least semi-annually.

Many dentists and physicians fail to make a complete and systematic examination of the oral tissues. When lumps or ulcers or changes in the character of the oral mucosa are detected, or when loosening of the teeth occurs, the dentist and physician are extremely likely to assume that the condition is inflammatory and that the cause is infectious. If every dentist can

be alerted so that he automatically considers the possibility of cancer in every mouth examination, great progress will be made toward the early detection and prompt treatment of this disease. A higher proportion of cures will surely result.

Why does the dentist not think of cancer? The reasons are partly psychological and partly statistical. The implications of cancer are so threatening and forbidding that most of us, consciously or unconsciously, tend to suppress thought of this disease. Then there is the very practical fact that cancer of the mouth is of rare occurrence, particularly in the mouths of patients who receive regular dental care. It has long been recognized that cancer is more prevalent in the ill-cared-for mouth containing broken-down teeth or poor dental restorations. Statistically, the incidence of cancer of all types is about three cases per 1,000 population. This means that if a dentist has 1,000 regular patients, he will be consulted by an average of three patients each year who will develop cancer. Only about one cancer in thirty, however, is a cancer of the mouth proper, that is, intraoral cancer. Therefore, among his 1,000 patients, only one in ten years, on the average, will develop mouth cancer. Nevertheless, the seriousness of the condition warrants a thorough visual and digital examination of the oral tissues, particularly in patients beyond the age of 40 years, although it must be remembered that cancer may occur even in children.

The American Cancer Society has spent a great deal of money on the establishment of cancer-detection clinics. When the results were analyzed, the cost per cancer discovered was in the vicinity of $10,000.00. No one can value a life or human suffering in terms of dollars alone. Nevertheless, the present program of transforming every physician and dentist's office into a detection center is a far more efficient and less expensive way of discovering cancer in its early and curable stages.

What, then, is the next step when the dentist once in five or ten years, perhaps, detects a lesion which, on clinical grounds, he considers to be cancer? The lesion may be one that the dentist has discovered during his examination, or perhaps it is discovered by the patient who then consults his dentist or physician. Patients with cancer of the mouth consult the dentist first in about one-third of all cases. With lesions on the gingivae, the percentage rises to as high as 50 or 60 per cent. The next step is establishment of the diagnosis by surgical removal of part of the tissue and its microscopic examination—in other words, the taking of a biopsy and its interpretation by the pathologist. In my opinion, the general practitioner of dentistry or medicine should immediately refer such a patient to a specialist for establishment of the diagnosis as well as for treatment. An experienced clinician can recognize squamous-cell cancer of the mouth with better than 90 per cent accuracy on clinical grounds alone, but the diagnosis must always be established by the pathologist's report. Otherwise, radical operations may be undertaken for the rare traumatic or inflammatory lesion which clinically simulates cancer. The

danger of false negative biopsies when material is removed by an inexperienced clinician is another reason that immediate referral to an oncologist is desirable. The manner and method of referral are of the utmost importance.

Great care should be taken not to alarm the patient unduly. A plan of action is outlined and immediately followed through. It is wise to avoid the term "cancer." One can speak of a "growth" or a "lesion." Patients will appreciate your honesty and thoroughness when you say: "There is something here about which I would like to have Dr. _____'s opinion. I will telephone him now and make an appointment for you to see him." You, the dentist, should make certain that the appointment is kept. If the patient asks if he has cancer, you can say: "No one can tell that without having tissue examined under the microscope. The chances are greatly against your having cancer; nevertheless, if cancer is present, we want to know it. Cancer, especially in its early stages, is curable. The first step is to see a specialist in the diagnosis and treatment of this disease."

Support and a positive program of action are essential. Many suicides occur in persons who fear that they have cancer and decide to take their own lives before the diagnosis is made. A near tragedy of that sort occurred in our university recently. An employee of another department was found in a comatose condition. His stomach was evacuated and he was subsequently sent to our clinic. A week before he had been told by his dentist that he had a mouth condition which "might be very serious." He was wearing an upper denture, the labial flange of which was cutting into the mucosa. The redundant tissue, called "epulis fissuratum," apparently suggested cancer to the dentist. Unfortunately, nothing positive was done. One of the patient's relatives had died of mouth cancer, and the patient was sure that the same fate awaited him, so he attempted suicide. When we saw him, he was assured that there was no clinical evidence of cancer but that the tissue would be removed for microscopic examination. The denture was left out for a week and the condition completely cleared up, so there was no need for even minor surgery. Subsequently, a new denture was made, and a partial lower denture as well, so that the condition would not recur.

The opposite danger, that of under diagnosis, has been with us for a long time. Many patients with advanced cancer of the mouth have consulted a dentist or physician and have been assured that the condition was of no importance. Often they have been treated by the physician with silver nitrate or by the dentist with gentian violet for periods of weeks or even months while the possibility of cure by surgery or irradiation was diminishing. It is a sound rule that any lesion which does not respond completely to treatment within a week or ten days should be considered cancer until the true diagnosis is established by biopsy.

The dentist or oral surgeon has a responsibility also to see that any clinically unusual material removed surgically is examined microscopically. It is a rule in many hospitals that all tissue removed surgically must be examined by the pathologist. We had one striking case in our clinic in which

a small nodule, not over 3 or 4 mm. in diameter, not ulcerated, clinically diagnosed as "granuloma pyogenicum," proved on microscopic examination to be an early cancer.

The white patches, or leukoplakia, of the oral mucosa constitute a particularly difficult clinical problem. Their treatment is notoriously unsatisfactory. It is well recognized that ulceration, fissuring, and induration are clinical signs that often indicate development of squamous-cell cancer. In dealing with leukoplakia, the dentist should remove all local sources of irritation, and should insist that smoking, the use of alcoholic beverages, and the consumption of spicy foods be drastically reduced or, even better, discontinued. Any white patch in the oral cavity that persists and becomes indurated, ulcerated, or papillomatous should be removed surgically and the tissue should be examined by the pathologist.

The dentist also should be alert to changes in the skin which indicate early cancer. Here he should function as a friend who suggests the importance of early diagnosis and treatment. Cancer of the skin is almost 100 per cent curable; so is cancer of the lip. Cancer of the mouth proper has a less favorable prognosis. The dentist should also know that hoarseness may indicate cancer of the larynx and that a "cigarette cough" may be a sign of cancer of the lung.

Now let us turn to the responsibilities of the dental profession where cancer of the mouth has been diagnosed. The dentist may aid the oncologist in preparing the patient for treatment, in the treatment itself, and throughout the post-treatment period. Careful oral hygiene, removal of calculus, removal of all sources of irritation, extraction of teeth in areas which will be subject to irradiation and which cannot be adequately protected by lead shields are the responsibility of the dentist. All dentists should be aware of the danger of operations of any kind, particularly the extraction of teeth, in tissues which have been heavily irradiated for cancer. Modern practice is to extract all teeth prior to treatment, if the teeth and jaws cannot be protected against irradiation. Extraction subsequent to irradiation may lead to serious and extremely painful osteoradionecrosis.

After treatment, the dentist may perform a great service in the rehabilitation of the patient by replacing excised tissue with prosthetic devices. These are the expert technical and engineering phases of dentistry. The dentist, with his knowledge of teeth and surrounding tissues and with his skill in the manipulation of materials, can contribute in a small but important way to the treatment and rehabilitation of the cancer patient.

Finally, we come to the realm of ideas. The cancer problem is not yet solved, and no one can be sure just what bit of observation may contribute to the solution of the problem. Dentists have played a not inconsiderable role in the development of anesthesia, surgery (including maxillofacial and plastic surgery), and prosthetic restorations not only for the teeth but also for nose, ears, eyes, and other parts of the anatomy. The dental profession has again made an important public health contribution in the prevention of dental caries by the fluoridation of drinking water. In the field of cancer, there is convincing

evidence that good oral hygiene does much to prevent the occurrence of cancer. In most laboratory animals, the oral mucosa is extraordinarily resistant to induction of cancer in contrast to the skin, where experimental cancer may be readily induced by a number of carcinogenic chemicals. Quite recently, however, the mouth pouch of the Syrian hamster has proved to be a site in which cancer tissue, including cancer of human patients, may be grown. Clinically, we know that cancer of the lip appears more frequently in pipe smokers and that cancer of the mouth proper occurs more often in cigar smokers and in persons who chew tobacco and betel nut. Many suggestions have been made concerning the effects of galvanic currents between dissimilar metals on the oral tissue, and certain metallic ions are carcinogenic. Clinical observations and research by dentists may, as in other fields, contribute in an important way toward solution of the cancer problem.

In summary, the dentist's responsibility in the diagnosis and treatment of cancer consists of performing his functions as an expert in the diagnosis and treatment of oral disease. By thorough examination of the oral tissues and associated parts, he will detect oral cancer in its early and curable stages. He should also allay cancer anxiety by his thoroughness and by his assurance that no abnormality exists when he finds none. When, in rare instances, he does locate a lesion which may be cancer, he is responsible for prompt referral of the patient for diagnosis and treatment. Once the diagnosis is established, the dentist is responsible for the establishment and maintenance of oral hygiene and for the extraction of teeth, where indicated, prior to treatment. The dentist may also assist in the designing and construction of applicators and protective devices used by the radiotherapist. He may contribute materially to the prosthetic rehabilitation of the treated patient.

The dentist should contribute to the ideas and factual knowledge which will one day solve the problem of neoplastic disease. When the control of cancer is realized, it will, like the development of the hydrogen bomb, have been the work of many people.

Paul E. Boyle

OPERATIVE ORAL SURGERY

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EXPERIENCES WITH SUBPERIOSTEAL IMPLANTS

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IT IS well known that the attempts to fix dentures mechanically to the alveolar process are very old. They have consisted of either (1) the implantation of root-shaped foreign bodies into natural or artificially created alveoli to which the dentures were fixed or (2) the stabilization of dentures by wiring them through or around the base of the bone. Such experiments were successful for only a few months or a few years, and they always ended in the expulsion of the foreign bodies. Most of the time this was accompanied by slow pus formation.[10] In 1940 Dahl,[1] from Sweden, had undertaken the first experiments to implant a metal framework not into the bone but underneath the soft tissue, with abutments emerging from the mucous surface to carry the denture. In spite of his failures, Gershkoff and Goldberg[3] continued with his idea and improved the technique. Thus, a metal framework was cast on a model, which had been relieved by an amount approximately the thickness of the soft tissues overlying the bone. The resulting failures were attributed to the insufficient fit of the framework on the bone, and a two-stage procedure seemed necessary. Later the bone was exposed at the first operation and, if necessary, corrected surgically for the taking of the impression. In a second operation, performed a few weeks later, the accurately fitting framework was inserted beneath the mucoperiosteum. Many cases were treated successfully by this method over a period of years, but still a certain number of failures occurred.

MATERIALS FOR IMPLANTS

The materials best suited for these implants are the chromium-cobalt-molybdenum alloys[12-14] (particularly Vitallium) and tantalum.[6] These materials had already been used successfully in general surgery as buried alloplastic implants. They best fulfill the demands for such properties as electric inertness, resistance to corrosion, insolubility in body fluids, and tissue tolerance; also, they are not cancerogenic, they are stable as a substance, they have the required hardness and stress resistance, and their properties are not changed by processing.

From Zürich University Dental School, Department for Oral Surgery (Prof. P. Schmuziger, Director).

CONSTRUCTION OF IMPLANTS

I prefer a netlike base, because of certain observations made in a case of tantalum implant reported by Marziani.[6] Five days after insertion of the tantalum base in that case, a part lay free over an area the size of a thumbnail. The expulsion of the implant was expected, but the contrary occurred. Granulations grew through the perforations; these united over the meshwork, and after three weeks a complete reactionless cover of epithelium had formed. Six months later, however, an abscess formed around the left molar abutment, which became loose and finally had to be removed. The same fate later befell the other abutments. Loosening of the abutments occurred because they were fastened with screws running through the perforations.

From this case, it was deduced that small metal strips forming a network may be covered by tissues, even if they are laid bare first, but this cannot occur when the implant framework consists of relatively wide bars. Moreover, it became evident that the framework and abutments must be one unit, so that the latter will not come loose. I have also confirmed the investigations of Früh,[2] who found that the kind of substructure used in this method, which can be adapted to the bone by pressure, may be deformed later by the forces of mastication. I therefore prefer a netlike framework with abutments cast in one piece.

An accurately fitting base can be obtained only if a direct impression of the bone is made previously. This makes a two-stage operation inevitable. The insertion of the implant may follow the primary operation by as little as eight to ten hours, which is the minimum time required to make the implant. Gershkoff and Goldberg,[3] Hammer,[4] and others, however, let three to six weeks elapse between the first and second operations. I did the same at first, but I could see that the fit of the implant is better if it is inserted one to three weeks after impression of the bone. A waiting period of three to five weeks may result in variable degrees of misfit, frequently causing spaces of 1 to 2 mm. between implant base and bone, while a waiting period of five weeks and more may result in such a poor fit that insertion would no longer be desirable. Originally, the impression was held responsible for such misfits, but comparative models obtained by impressions made at the first and second operations clearly showed that bone resorption is due to the mere fact that the bone has been exposed. The following case may illustrate this.

A patient, for professional reasons, came three months after the first operation to have her implant inserted. The fit of the implant was so poor that it could not be used. Therefore, a new impression was made. Unfortunately, the patient again waited three months, and again there were in certain places spaces of as much as 2 mm. between the implant and the bone. It is possible that this bone resorption induced by exposure of the bone is arrested after insertion of the implant. On the other hand, it is equally possible that resorption goes on until the blood circulation becomes normal again and a stationary condition is reached. Only thus is it possible to explain the fact that a distance of 1 to 2 mm. from implant to bone can be seen

roentgenographically in almost all cases. Naturally, such a space can be recognized more readily if a framework with meshwork structure is used instead of that used by Gershkoff and Goldberg[3] and others.

FIXATION OF IMPLANTS

It is almost universally recognized that it is not necessary to wire or screw the framework to the bone.[8] With adequate preparation of the bone and sufficient extension of the implant framework, the latter is held sufficiently well during the initial postoperative period, and after eight to ten days it is already fixed by connective tissue. A supplementary fixation is necessary only in exceptional cases, particularly in maxillary cases. In such cases, the implant is secured by peralveolar wires or wires looped around the mandibular bone and over a plastic bar, placed over the abutments of the implant, which can easily be removed after ten days.

HEALING OF TISSUE

The healing tendency of the tissues over a subperiosteal implant, although it may appear unsatisfactory at first, has been excellent in every case, even without antibiotic protection. The most important step is to close the wound margins perfectly over the implant. I use the continuous horizontal mattress suture for this purpose.

COMPLICATIONS

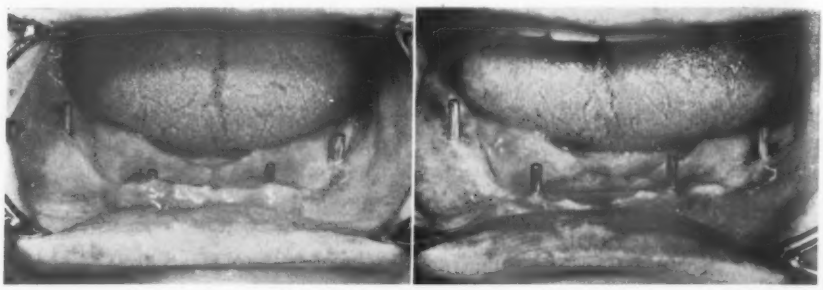
It is important to study the complications which have occurred, since we can learn a great deal from them.

1. *Dehiscence of Wound Edges.*—After either the first or the second operation, the wound edges may separate. The reason may be insufficient vascularization because the incision line was placed too far to the vestibular side. The consequences are increased bone resorption and therefore poor fit of the implant. Additional reasons for separation may be inadequate suturing or infection of the wound margins. Freshening of wound margins and secondary suturing, however, may promote healing without complications for as long as one week after insertion of the implant. Another cause of separation is a postoperative hematoma. In a case of partial maxillary implant, we have observed a primary exposure of the implant base caused by this complication.

2. *Calculus Formation.*—Calculus may form on the abutments as well as on natural teeth. Insufficient cleaning or leaving the denture out for too long a period of time may cause the formation of such deposits.

3. *Pocket Formation.*—The question of pocket formation has been the subject of wide discussion. Beyond any doubt, it occurs. First, there is the *primary pocket formation* of surgical origin. We know that after gingivectomy there forms around the base of the abutment a strong scar of connective tissue which seems to give a good closure (Fig. 1, *A* and *B*). In order to avoid this primary pocket formation, I perform a prophylactic gingivectomy when I insert the implant.

Primary pocket formation is also possible if the abutments are placed too far buccally or lingually. Then the pressure of the soft tissues causes an ulceration. Partial plastic repair of the sulcus is necessary in such cases. This consists of the dissection of the soft tissues overlying the implant framework, fixation of the mobile wound margin in the vestibular sulcus, and self-healing of the wound, which eliminates this undesirable condition.



A. *B.*

Fig. 1.—Primary pocket formation of surgical origin, before (*A*) and two years after (*B*) gingivectomy around the posts.

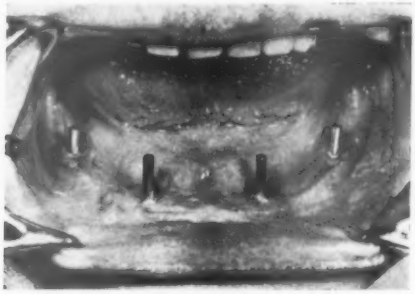


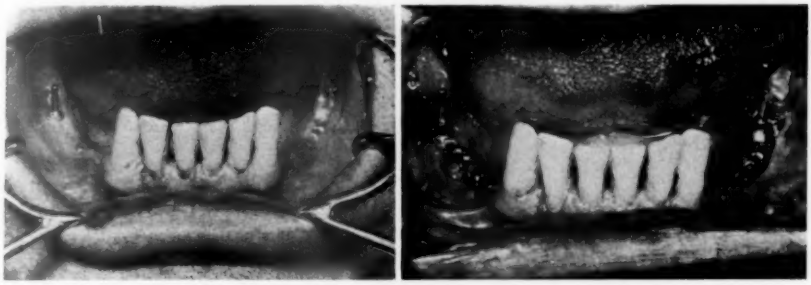
Fig. 2.—Secondary pocket formation at the post in the right molar region. The fistula at 4- appeared when the pocket formation at the post of 3- disappeared.

On the other hand, pocket formation in the sense of a periodontal pocket forming because of the absence of a true attachment to the abutment post has been observed repeatedly. We call it a *secondary pocket formation.* It is a progressive development in which the metal framework is the leading element for the pocket. The latter may enlarge buccally or lingually. In such cases (Fig. 2), the soft tissues in the neighborhood of the abutments become slightly inflamed and swollen, and an anesthetic injected 5 to 10 mm. away from the abutment emerges unhindered at the site of the abutment. When this occurs, neither gingivectomy nor antibiotic therapy is of any permanent value. This condition may appear to have healed if the secretion is expelled by a nearby fistula.

4. *Lack of Proper Alignment of the Abutments.*—If the abutments are not parallel, the one out of alignment has to be shortened. In order to avoid this,

the laboratory must be asked to produce and furnish the removable bar at the same time as the implant frame.

5. *Exposure of the Implant Base.*—Exposure should certainly be considered a complication. If an exposure were to develop with a buried implant in general surgery, one would certainly speak of it as a failure. The framework may be exposed primarily because of rupture of the suture or a hematoma, as discussed before, or it may become exposed gradually. In the case shown in Fig. 3, there was a narrow alveolar crest which was not sufficiently reduced, and too much time elapsed before the implant was inserted. It was found that it did not fit properly because the reactionless covering of soft tissue seems to have adapted itself closer to the bone, through the mesh of the framework,



A. *B.*

Fig. 3.—Exposure of implant base. *A*, Condition three months after insertion of the implant. *B*, Condition two years later.

Fig. 4.—Acute abscess formation in an implant case.

and the latter was thus exposed within three months without any inflammatory reaction of the mucoperiosteum (Fig. 3, *A*). The space between the base and the bone had increased, and now two and one-half years later practically half the framework is exposed (Fig. 3, *B*). Such exposure may start even as late as three years postoperatively. We could observe this in a case and believe that this complication occurs because of a gradually developing bone resorption which is being followed by the overlying soft tissue without being hindered by the implant frame.

6. *Abscess Formation.*—We have observed acute abscess formation. Fig. 4 illustrates such a formation, which is similar in appearance to a progressive

apical abscess. Still more frequent are abscesses resembling periodontal abscesses, especially the relapsing subacute-chronic form. In other instances, one may observe a subacute or chronic inflammatory infiltration around a post, mainly on the buccal side in the molar region (Fig. 5). Each of these infections ultimately forms a fistula. The pus discharges along the abutment or from a fistula on the margin of the implant.

7. *Fistula Formation.*—Fistulas form as described or without previous abscess or pocket formation. A fistula may simply develop without symptoms of pain. It appears suddenly. Fig. 6 shows a case in which such a fistula appeared more than six months after insertion of an implant without the denture having been inserted, that is, without stress on the implant. Later, two other fistulas appeared posteriorly, also without causing symptoms.

8. *Breakage of an Abutment.*—This most unwelcome complication is due to faulty casting or to unfavorable stresses acting on the abutments. Roentgenographic checkup of the finished casting is therefore indispensable.[14]

Fig. 5.

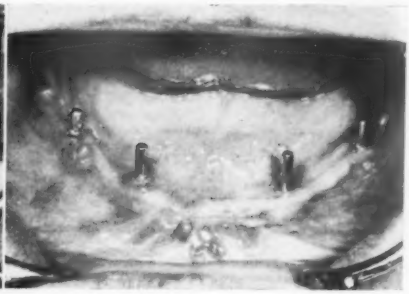


Fig. 6.

Fig. 5.—Relapsing subacute-chronic inflammatory infiltration around the post in the molar region with swelling and pain.
Fig. 6.—Fistula formation in the region of 8–, 5–, 1–, –7.

9. *Bone Resorption.*—This occurs with and without signs of damage to the bone contour. The cause may be a disturbance of circulatory conditions, an inflammation, pressure, or lateral stress, or the resorption may be merely a physiologic process. Demonstration of resorption of bone in an advanced stage is simple, but it is difficult to demonstrate it in an incipient stage. One symptom is a decrease in vertical dimension, but it is difficult to register such a decrease accurately. While the roentgenogram is the best means for diagnosing bone resorption, mistakes in projection must be avoided. Certain proof is the formation of steps in the bone line, as shown in Fig. 7. Control films taken at certain intervals can also be used to prove that a reduction of bone has taken place, even without damage to bone contour itself. Such cases have been published by Naucke,[8] who used an implant framework as suggested by Gershkoff and Goldberg.[3] In the first roentgenogram of one of Naucke's cases one sees unmistakably the mental foramen, which five years later cannot be seen because it is covered by the implant base. The patient had a complete anesthesia of the mental nerve, a symptom which can occur only when extensive bone resorption allows the metal frame to compress the nerve. Considerable

loss of bone beneath the base of the implant after good initial fit is also a reliable criterion, as has been demonstrated by Schmidt.[11] On the other hand, bone resorption may be suggested by a roentgenogram if the implant, by unfavorable stresses from the denture, was levered off its bony base. Fig. 8, *B* shows this beyond any doubt, and the corresponding clinical photograph (Fig. 8, *A*) shows extensive exposure of the framework. On the other hand, a

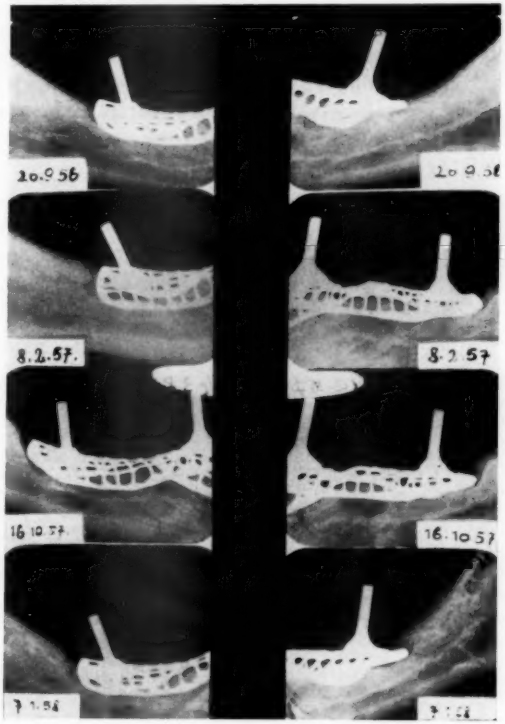
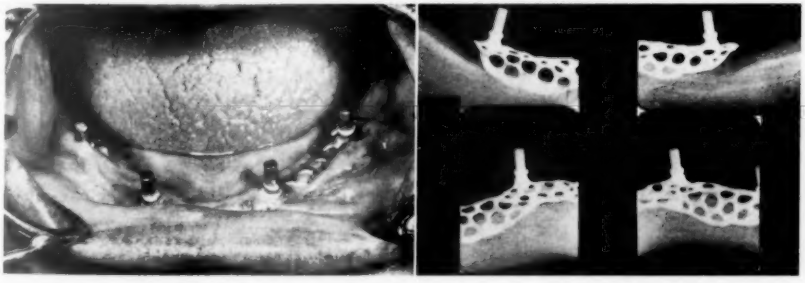


Fig. 7.—Step formation in bone contour as sign of bone resorption.



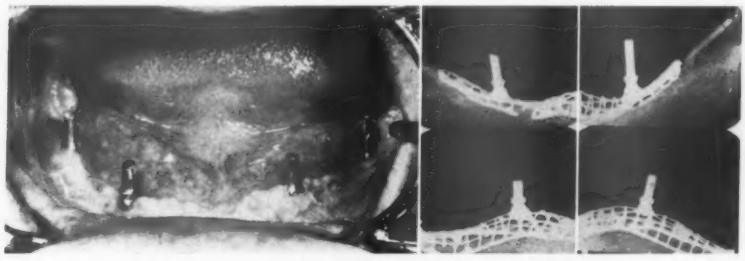
A. *B.*

Fig. 8.—Elevation of implant base because of unfavorable stresses from the denture (*A*), suggesting bone resorption (*B*) as seen in the roentgenogram.

combination of both true resorption of bone and leverage of the implant may occur. It is clear that after sufficient experience complications may be partly avoided, but most of them can occur even when the utmost care is taken. A complete x-ray examination, including posteroanterior and lateral projections, is indicated in every case in order that an impacted third molar, a residual granuloma, or a cyst be not overlooked.

SUCCESSFUL CASES

So far, good results have not been discussed to encourage the use of implants. Naturally, a number of beautiful cases could be cited, although we do not know why in these there were no complications. One case is of special interest, however. It seems to discredit currently accepted rules. We inserted the implant three years ago and did not know at the time that merely exposing the bone would cause bone resorption. On insertion three and one-half months after bone impressions, there was a space of up to 3 mm. between the implant and the bone in the frontal alveolar region. So far, in spite of this, the case is clinically and subjectively a complete success (Fig. 9, *A*). In the corresponding roentgenogram one can easily see a misfit of the framework in the front (Fig. 9, *B*).



A *B*

Fig. 9.—Clinically perfect result for three years (*A*), in spite of very bad fitting of the implant base in the front area when the case was inserted (*B*), as shown in the roentgenogram.

PROSTHETIC REPLACEMENT

Although perfect retention may be obtained with an implant, the denture construction must be carried out with even more care than in the case of an ordinary denture. This fact has been stressed particularly by Marziani.[6] Even the slightest fault in articulation or in muscular equilibrium may cause a lot of trouble.

We are fortunate that our patients are receiving superb prosthetic treatment by Professor Gerber, director of the Prosthetic Department of the Zürich Dental School, so that complications due to faulty articulation, such as that shown in Fig. 8, do not occur. Collaboration between the surgeon and the prosthodontist has proved to be of great importance in planning the implant framework, the extent of coverage, and the localization of the abutments.

SUMMARY

The following results have been obtained in the department of Professor Schmuziger in the Zürich Dental School: Thirty-five implants were inserted in thirty-three patients; of these, there were twenty-three total and two partial mandibular cases and eight total and two partial maxillary cases. A follow-up examination after one to one and one-half years showed that one-third of the cases developed complications such as those mentioned previously. A checkup after one to three years on thirty-three cases showed complications in two-thirds of the patients. Four patients had acute swelling around one or more abutments due to catarrhal infection, five patients presented chronically inflamed infiltrations and subacute infections in the neighborhood of the abutments, four developed acute abscesses, fistulas formed in four, eleven had discharging pockets along the abutments, six had partial exposure of the substructure, two had fractures of the abutments, and three developed hypesthesia or paresthesia of the mental nerve. In three cases former swelling did not recur; in two cases former fistulas have disappeared, but discharge along the abutments has developed instead. In one case the implant had to be removed because of massive foreign body reaction due to application of nonresorbable Aureomycin powder. In all, nineteen cases show imflammatory reactions at the present time, while thirteen are without notable inflammatory symptoms, clinically and subjectively. Two of these have paresthesia, one has hypesthesia of the mental nerve, and one patient complains of pains on changes in the weather. Thus, of thirty-two implants inserted more than one year ago, only nine have remained clinically and subjectively intact.

Our results are about the same as those obtained at other European clinics,[8, 9] but it seems that the determination of success or failure depends on the way of looking at it. Only thus can it be explained that, for instance, Maurel,[7] Trainin,[12, 13] Marziani,[6] and others speak of almost 100 per cent success. Before every operation one should remember, as Kallenberger and Mäglin[5] pointed out, that a denture implantation is a nonbiologic procedure. The good results in animal experiments are not unconditionally transferable, since most of the animals have been wearing their implants for only a few months or a few years; no dentures were ever placed on such implants, and therefore they did not have to bear the stresses of mastication. Most of the complications described here occurred only after prosthetic rehabilitation and could be partly eliminated by simply leaving out the dentures. Therefore, it seems easier to insert an implant successfully than to construct the prosthetic replacement in a way that does not turn the case into a failure. It is easy to promise that the patient can chew for several more years with the help of an implant, but in our opinion it is impossible to promise that, even after twelve months or so, there will be no complications which theoretically would make the implant rejectable from the medical point of view. Thus, according to our experiences, implants are indicated only when they are expected to serve for a limited period of time.

Even in the face of the fact that almost two-thirds of our cases are showing complications which must be expected, on the basis of biologic knowledge, we must try to clarify the question of why these complications did not appear in the remaining third. Thereby, and after elimination of the difficulties with which every beginner is faced when using a new method, the rate of success is certain to improve with experience. This is why, in my opinion, the experiments with implants should be continued as a research project in suitable cases in certain teaching centers.

I wish to express my gratitude to Professor A. Gerber, Director of the Prosthetic Department, and to Professor P. Schmuziger, Director of the Department of Oral Surgery, Zürich University Dental School, for their great help and collaboration in this field of work and to Raoul H. Boitel, D.M.D., D.D.S., of Zürich, for his great help in the translation of this paper.

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INTRAORAL TITANIUM IMPLANTS

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ADJUNCTIVE or definitive procedures in oral rehabilitation require, at times, the fabrication of appliances of special design, such as the intraoral implant. At present the austenitic alloy is the one material of choice, although acrylic, polyethylene, and tantalum metals have been used. However, there is a definite need to evaluate the possibilities of the use of another available metal, titanium, as a submucoperiosteal insert in the field of dental surgery.

The significance of this research lies in its possible contribution to the rehabilitation of persons in whom ontogeny, disease, accident, or type of therapy has altered or destroyed the normal condition of contour, bulk, or position of the tissues of the mouth or face. When emendatory procedures requiring surgical adjunctive appliances and/or definitive prostheses are limited to the use of a very small number of materials, problems of availability, cost, etc. may arise. Materials in use may also exhibit less desirable physical properties under certain conditions of environment or manipulation. Therefore, when another stock manifests greater utility under certain situations, it should be explored. This stockpiles effectual resources and often opens up new avenues of application.

This research project is a continuation of previous investigations[2, 3] initiated in 1954, which have proved that implanted titanium metal is inert and completely tolerated by living tissue. This compatibility is with soft tissue and bone, demonstrated in the animals in which the metal was placed as a disk into muscle tissue, as a plate to unite a fracture (femur of a dog), and as a plate over a trephined area of the skull. Stress was present in the fracture area, there was physiologic movement in the muscle, and essentially no stress was present in the skull.

In this report, for the sake of ratiocination, it is necessary to present a relatively thorough discussion of the metal itself as well as the experimental studies. Therefore, the presentation will be in two parts: (1) the history of titanium, its characteristics, and the management required and (2) the experimental work that has been done using titanium as an intraoral implant in areas of bone loss and under conditions of stress and nonstress.

From the University of Washington School of Dentistry.
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HISTORY AND PROPERTIES OF TITANIUM

History.—Titanium, a silvery gray metal, the ninth most abundant in the world,[5] was discovered more than 160 years ago by the Rev. William Gregor, an amateur mineralogist. Gregor analyzed a black, magnetic sand from an area of Menaccen in Cornwall, England, and found that it contained a new element. In his account of the investigation, published in 1791, he called this element menaccanite.[13] About five years later, M. H. Klaproth, a German chemist, studied the composition of the mineral rutile (TiO_2) and found what he supposed was a new element. He named this element titanium after Titans of Greek mythology.[7] Later, in 1797, Klaproth examined some ilmenite ($TiFeO_3$), the same black sand mineral that Gregor had studied, and realized that his element and menaccanite were the same. The name titanium persisted, probably because the precedent for using mythologic names for scientific discoveries had been well established. Many attempts were made throughout the nineteenth century to produce titanium metal from its compounds, with some success finally occurring at the end of this period. During the early part of the twentieth century there were numerous investigations of the physical and mechanical properties of the metal, with increasing interest in the metallurgy of titanium becoming widespread during World War II.[13]

Recovery From Its Ores.—The ore is crushed, ground, and separated from extraneous material by flotation, specific gravity, or magnetic methods,[13] the latter being preferred. This leaves titanium dioxide, which is reduced with chlorine to form titanium tetrachloride, in turn treated by the Kroll process[10] to change it chemically by reduction with magnesium in an inert atmosphere (argon or helium) or in vacuum to form titanium sponge. There are other methods of producing pure titanium on an experimental basis, but the Kroll process is the most feasible at this time and is used by most of the commercial producers of the metal. The cost of producing the sponge form of titanium is being reduced with its constantly increasing production and was $3.95 a pound in 1956.[13]

Melting, Casting, and Molding the Materials.—The high melting point of titanium (3,140° F.) and the highly reactive nature of the element make the melting and casting of titanium a difficult problem. Kroll observed that at temperatures of a few hundred degrees Centigrade, titanium will absorb oxygen, nitrogen, and hydrogen,[10] all of which severely reduce the ductility of the metal and make it brittle. To avoid contamination, therefore, procedures must be carried out in a vacuum or in an atmosphere of inert gas. This requires modification of the established melting and casting techniques used for most other metals.

Induction melting and electric arc melting are the two most common methods used at present, the latter being preferred for commercial production. For small-scale procedures, the induction melting method is desirable, since it is possible to melt the metal titanium in a graphite crucible,[1] even though a reaction (in the form of vaporized carbon) between the graphite

and liquid titanium does occur. This reaction can be reduced by coating the graphite with titanium carbide, by dipping in liquid titanium, or by covering the crucible with powdered titanium and heating in a vacuum.

Two methods of casting that appear to be satisfactory[11, 12] have been developed. The first is shell molding (forming two metal cavities, one-half on each side of the pattern of the part to be cast, which are coated with a resin-refractory mixture to form the mold). The second is investment casting, with which the dental profession is familiar. A pattern of wax or plastic is fabricated, coated with zirconia (zirconium dioxide) and zirconium nitrate as a binder, air dried, heated for one to two hours at 1,500 to 1,600° F., and air cooled; the mold is sealed to the furnace, and the casting is made.[1] Other expendable mold materials utilize graphite[8] and zircon (a compound of zirconium silicate) plus phenol formaldehyde and ammonium silicofluoride, the former acting as binder and the latter as inhibitor.[15] Ideally, any expendable mold should be economical, easy to form, and inert to the liquid titanium

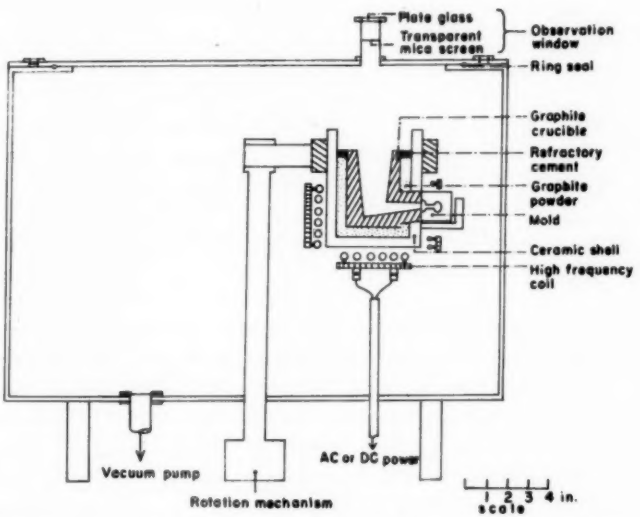

Fig. 1.—Sketch of combination titanium furnace and casting machine in vacuum chamber as modified by W. J. Ploger.

which may be near 4,000° F. when it hits the pattern mold. Pickling of castings is accomplished by immersion in a bath of 48 per cent nitric acid and 2 per cent hydrofluoric acid.[21] Considering the intricacies and dimensional limitation in the field of dentistry, a centrifugal casting machine (which is feasible and has been successfully developed on a commercial scale),[4, 19] combined with a graphite crucible furnace contained within a vacuum chamber[9] may be designed, as illustrated in Fig. 1, and constructed to facilitate further research in the use of titanium in the dental field. At present, the metal is

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received in rod, bar, or sheet form of various dimensions and must be hand-worked or machined into the forms desired—a time-consuming and relatively expensive procedure at present. It should be noted that the commercial producers attempt to mill to as near requested dimensions as possible.

Properties.—Titanium's lightness in weight (44 per cent lighter than steel), strength (almost that of steel), low thermal conductivity, and heat resistance are desirable properties, as shown in a comparison of the properties of titanium, tantalum, stainless steel (austenitic), gold (dental alloys), and Vitallium (stellite), as given in Table I.

TABLE I. COMPARISON OF THE PROPERTIES OF TITANIUM, TANTALUM, STAINLESS STEEL, GOLD, AND VITALLIUM

PROPERTIES	TITANIUM[17]	TANTALUM[18]	STAINLESS STEEL[14] (AUSTENITIC)	GOLD[14] (DENTAL ALLOYS)	VITALLIUM[14] (STELLITE)
Density (Gm./c.c.)	4.5	16.6	7.92	14.6-19.3	8.3
Tensile strength, (lb./psi)	80-110,000	50,000	87,000	30-120,000	60-101,000
Thermal conductivity (BTU/ft.^{2}/in./° F./hr.)	105	378	115	700	145
Elongation, 2 inch gauge length	15-25%	40%	55-60%	20-35%	16%
Atomic number	22	73	(26)*	(70)†	—
Atomic weight	47.88	180.88	(55.85)*	(197.2)†	—
Melting point (° F.)	3,140	5,425	2,600	1,600-1,945	2,547
Specific heat (cal./Gm.)	0.13	0.036	0.12	(0.031)†	0.11
Brinell hardness number	180	150	135-185	45-235	142-157

*For pure iron.
†For pure gold.

Ductility is affected with the absorption of nitrogen, oxygen, and hydrogen, making the metal brittle. Hydrogen, unlike carbon and nitrogen (which harden the metal), can be removed by heating the metal in a vacuum at elevated temperatures,[6] while oxygen forms a protective oxide surface resulting in corrosion resistance (like that of platinum).

It has been found that care must be exercised in cutting or grinding this metal to avoid overheating or work hardening. These procedures require slower cutting to prevent seizing (tendency to bind), galling (friction welding of the metal chips to the cutting blade), and rapid deterioration of the cutting blade. Grinding can be done with an alumina wheel (plus a coolant), coarse grinding papers, and emery papers. Polishing must be done carefully to avoid pitting or flowing of the metal during this step of the procedure. Therefore, a lubricant must be applied to the metal surface while high-speed, heavy pressure is being used with a polishing period of short duration and final buffing with soft cloth.[13]

There are certain safety precautions to be borne in mind in handling titanium, even though the quantity handled on a laboratory basis may be small. Titanium metal powder, like other metal powders, is highly pyrophoric, with

consequent necessary precautions of adequate ventilation and lubrication during cutting, grinding, or polishing. Liquid titanium metal burns vigorously in air and should be controlled by using dry sand or an inert gas, such as argon or helium, to extinguish the fire.[16, 20]

EXPERIMENTAL STUDIES IN DOGS

Previous investigations have demonstrated that titanium metal is inert when implanted into muscles and into or onto bones of dogs and that adjunctive and definitive appliances of the metal are acceptable to both bone and soft tissue with no sign of infection or inflammation. As a continuation of this work, the present project was undertaken.

Object.—This study was undertaken to determine (1) whether a titanium plate used with titanium nuts and bolts may be used for reduction and stabilization of the posterior and anterior segments of an ostectomized mandible of a dog and (2) whether a hiatal defect in the palatal bone of a dog can be closed permanently with a titanium disk.

Methods of Procedure.—Initially, radiographs were taken prior to any surgical procedures to (1) evaluate the areas to be operated upon and (2) serve as guides in the construction of the titanium implants. Lateral oblique roentgenograms were taken of dogs A and B to obtain the outline of the mandible to be used as a guide for the final fabrication of the plates, while a superior view through the palate was taken to determine a location for the implantation of a disk in dog C.

Nembutal sodium, in a concentration of 60 mm. per cubic centimeter, was administered in a dose of 0.5 c.c. per kilogram of weight into one of the veins of a leg to anesthetize each dog.

A liquid diet of milk and water was given for the first five days postoperatively, with a gradual change-over to a soft diet (composed of dog meal, milk, and horse meat) to all dogs involved in these experiments.

Dog A: Under surgical asepsis, an incision was made on the left side of the mandible, on the buccal and lingual tissue surfaces, 4 to 5 mm. below the free gingival margin, extending from the cuspid to the third molar. The mucous membrane and periosteum were lifted to expose the buccal and lingual aspect of the mandible as well as to free the inferior border of this bone. The titanium plate (1.6 mm. thick, 12 mm. wide, and 56.6 mm. long) was used as a template to position the holes for the bolts (2.8 mm. thick and 17.5 mm. long, the nuts being 3.3 mm. thick and 5.2 mm. wide) on the cortical bone (Fig. 2). These locations were marked on the bone, and the holes were then formed with an electric hand drill. A Gigli saw was placed between the tissue and the bone on the lingual aspect and an ostectomy of the mandible was performed to include the third premolar, being wider superiorly than inferiorly. When the titanium plate was positioned, it was found that the second hole from the anterior of the plate was too close to the cut edge of the mandible, and another hole was drilled closer to the first hole, with saline

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used as a coolant. The plate was bolted into place, the occlusion was checked, and the area débrided. The latter was then closed with catgut suture material along the buccal and lingual incisions and across the socket area. A postoperative roentgenogram showed the cleanly cut borders of the mandible (Fig. 3).

Fig. 2.

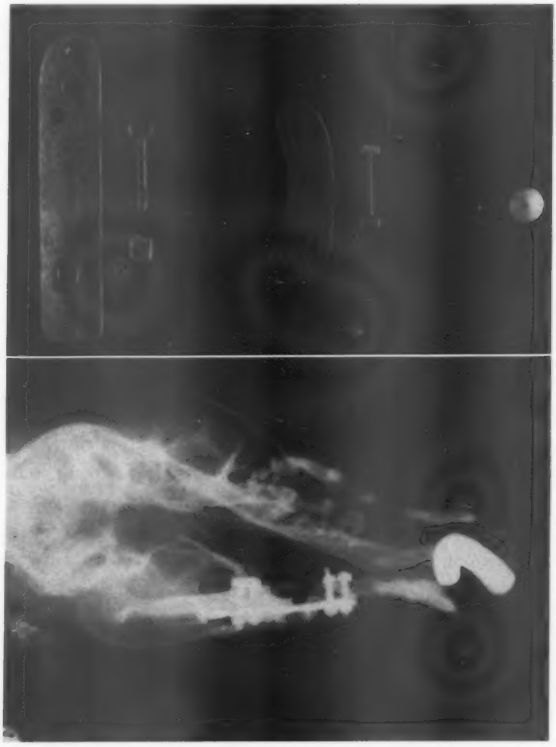

Fig. 3.

Fig. 2.—*Left to right:* The titanium plates, nuts and bolts, and disk used in dogs *A*, *B*, and *C*, respectively.
Fig. 3.—Immediate postoperative roentgenogram of dog *A*.

Dog B: This dog was operated on under similar conditions of anesthesia and surgical asepsis, except that the initial incision on the left mandibular ramus included the gingival papillae and extended again from the cuspid to the third molar. After complete buccal and lingual flaps were lifted and the inferior border of the mandible was freed from the periosteum, a Gigli saw was used to remove the third premolar and its contiguous portion of the mandible (Fig. 4), as was done in dog A. A titanium plate of irregular shape (1.6 mm. thick, 9 to 10.8 mm. wide, and 33.5 mm. long) was again used as a template to mark the holes for the bolts (1.5 mm. thick and 15 mm. long, the nuts being 1.7 mm. thick and 3.7 mm. wide) (Fig. 2). These holes were made

with a 703 surgical bur in a straight handpiece prior to the ostectomy. After debridement and suturing with catgut, the area of surgery appeared as depicted in Fig. 5.

Fig. 4.—Ostectomized left mandibular segment of dog *B* with third premolar in situ.

Fig. 5.—Appearance of operative area of dog *B* after closure.

Dog C: With similar operative technique prevailing, a palatal incision 5 to 6 mm. from the median line and lingual to the first maxillary left molar was made, running about 25 mm. in length anteroposteriorly. The periosteum was elevated laterad to expose the palatal bone, and cautery was used to stop the extensive venous blood flow. A round surgical bone bur in a straight

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handpiece was used to perforate the palate, creating a communicating defect about 6.5 mm. in diameter. The nasal outline of the opening was of smaller diameter than the palatal aspect. A titanium disk, 0.4 mm. thick and 6.6 mm. in diameter (Fig. 2), was placed over the hole that was surgically created so as to rest against the nasal cortical bone of the palatal opening. The flaps were drawn over the area and sutured with catgut.

Fig. 6.—Exposure of titanium appliances due to tissue slough after eighth postoperative week in dog *A*.

Observations and Results.—

Dog A: For the first four weeks postoperatively, the healing progress of the area appeared to be satisfactory. Toward the end of the fifth week, a slight tissue slough was noted on the buccal aspect in the area of the second premolar. Antibiotics were administered for three days, daily saline rinses were used for the next two weeks, and vitamins A and D were added to the soft diet. By the end of the sixth week, 2 to 3 mm. of the titanium plate, slightly distal to the second premolar, was exposed with part of the mandible on the lingual aspect anterior to the fourth premolar. During the seventh week, the exposure of the superior edge of the plate was approximately 5 to 6 mm. and the anterior nuts were slightly perforating the buccal tissue. One week later, the eighth postoperative week, the titanium was exposed one-fourth of the total length of the plate on the buccal aspect and the superior edge was completely exposed over the area of ostectomy, with an extension of 3 to 4 mm. down to the lingual side of the plate. The tissue covering the severed ends of the mandible appeared healthy and seemed to fold down into the area of ostectomy and blend in with the floor of the mouth (Fig. 6). A roentgenogram of the area showed that resorption had occurred toward the

lingual side (Fig. 7). There was slight mobility of the plate and of the posterior segment of the mandible. The ninth week found the posterior nuts exposed and the anterior portion of the plate almost entirely exposed. By the end of the twelfth week the exposure of the buccal aspect of the entire titanium plate was complete, and no change in the degree of mobility was noted. Humane sacrifice of the dog was made at the end of the fifth postoperative month with the plate exposure, degree of mobility, and tissue conditions remaining the same. Upon débridement of the soft tissues from the mandible, it was found that osteoclastic activity had occurred around the nuts and bolts and in between the roots of the second premolar and the fourth premolar.

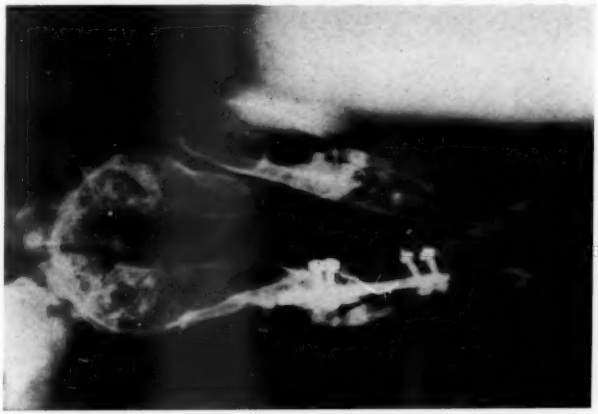

Fig. 7.—Roentgenogram of dog *A* eight weeks after surgery. Exposure taken with dog's head against plate.

Dog B: Postoperatively, the healing pattern was similar to that of dog A, with a slight tissue slough appearing by the end of the fourth week, as pictured in Fig. 8. The rate of exposure of the titanium plate was similar to that of dog A, with radiographic evidence of bone resorption at the end of seven weeks (Fig. 9), with slight mobility of the plate and posterior mandibular segment noted at this time. Upon sacrifice of the animal and soft tissue débridement of the mandible, osteoclastic activity of the same type and extent as in dog A was found.

Dog C: One week postoperatively an area of grayish discoloration about 6 mm. in diameter in the midline of the incision was noted. This discoloration persisted during the second week and took on a dull pink appearance by the end of the third week, extending 3 to 4 mm. along the length of the original incision. This pinkish hue continued for the next three weeks and gradually returned to a normal color (Fig. 10). Follow-up examination at the present time reveals that on palpation the disk cannot be felt and the overlying palatal tissue shows a scar in the area, with the tissue being of firm, healthy, and

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normal consistency. Roentgenographic evidence shows no signs of bone resorption. As in our previous investigations, it was noted that the metal disk was radiolucent (Fig. 11).

Fig. 8.—Exposure of titanium appliances due to tissue slough after fourth postoperative week in dog *B*.

Fig. 9.—Roentgenogram of dog *B* seven weeks after surgery. Exposure taken with dog's mandible against plate.

Discussion of Results.—The results in dogs A and B may be considered unsuccessful, due to one or a combination of the following factors: (1) The surgical technique or approach may have been too traumatic. (2) Stabilization of the mandible may have been unsatisfactory, so that the plates were moved by the forces of mastication, swallowing, barking, etc. (3) The titanium

plates and bolts may have been of too much bulk and thickness for the thin mucous membrane and intraoral connective tissue coverage and facial musculature of the dogs. On the lingual aspect of the mandible, where there was greater bulk of tissue, the titanium nuts were accepted without indication

Fig. 10.

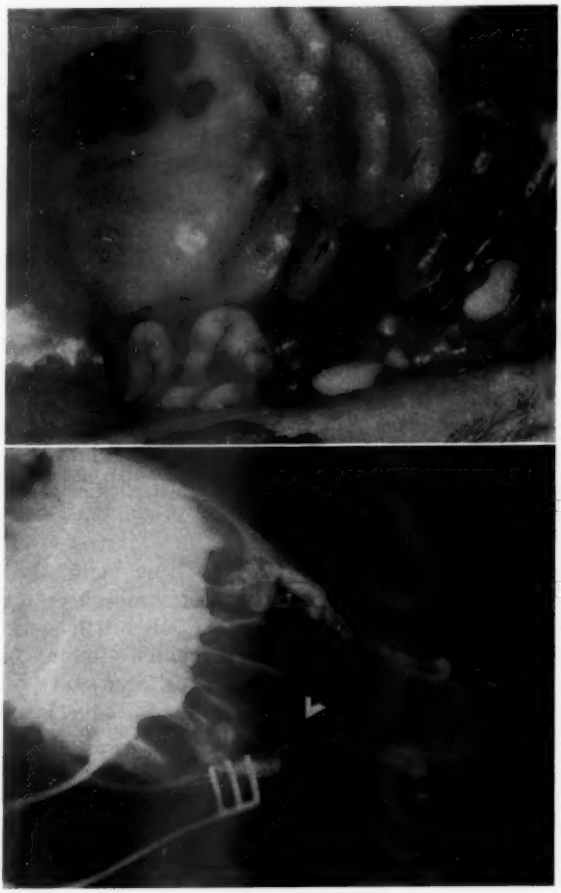

Fig. 11.

Fig. 10.—Appearance of operative area of palate of dog *C* seven months after implantation of titanium disk.

Fig. 11.—Roentgenogram of dog *C* seven months after implantation. Arrow indicates site of disk, which is radiolucent.

of tissue breakdown. (4) Adequate protection of the surgical area by the use of an acrylic splint which could be kept in place without dislodgment by the paws of the dogs was lacking. (5) The superior edges of the plates and buccal nuts provided an anvil-like base against which the thin tissue

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covering may have been traumatized during mastication. (6) We failed to provide a nucleus or matrix for osteoblastic activity in the ostectomized area. Contributing factors to the negative results of this type of procedure are (1) immobilization of the mandible via the maxilla cannot be accomplished as readily in the dog as in the human being and (2) feeding the dog through an esophageal tube placed through the nasal passage is difficult from a practical standpoint. The fact that osteoclastic activity had occurred, with resultant mobility of the plate and posterior segment of the mandible, may have been due to the forces of leverage as a factor in the bone resorption.

Dog C indicates that there has been complete acceptance by the tissues and palatal bone and that the procedure used was successful. The delay in the rate of healing and scar formation possibly may be attributed to the cauterization that was required.

SUMMARY

Titanium.—The importance of the relative abundance of this metal has been almost overshadowed by the problems associated with recovering it from its ore in a form of high enough purity to take advantage of its properties. Titanium is light in weight with a strength comparable to steel, giving a greater strength-to-weight ratio than any of the alloys (of cast form) now used in the field of dentistry. The low thermal conductivity of this metal is of such significance that further research of its potential uses in the dental and medical fields is warranted. It is economical to produce, with the cost factor decreasing with a constantly increasing production, and it is lower in cost than metals now used clinically.

At present, the disadvantages of high melting point, the necessity for completing the casting procedures in an inert atmosphere or vacuum, the absorption of gas during processing with resultant brittleness, the obtaining of mold materials that will not react with molten titanium, and the care necessary in finishing are problems which need further study. (This is being continued by various manufacturers of titanium products and the United States Department of Interior Bureau of Mines.)

Use of Titanium as an Intraoral Implant.—The results of the experiments in dogs A and B indicate that a better technique of surgical approach, protective mandibular stabilization, and construction of an appliance of different design may be necessary to permit tissue adaptation without the resultant tissue trauma and leverage action previously described. Since the titanium disk implant indicates acceptance by the palatal tissues and bone in dog C, and since previous investigations have proved the inertness and tissue tolerance of the metal, it is felt that further investigation would be of merit. Such is being continued.

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AN EVALUATION OF THE PRESENT STATUS OF IMPLANTODONTICS

Leon Herschfus, D.D.S., Detroit, Mich.*

DURING the past decade the rapidly growing field of implantodontics has been filled with countless conflicting and contradictory reports which have left the investigator and clinician somewhat perplexed and bewildered.

Part of this confusion may be attributed to the introduction of methods of approach based on theory and speculation instead of established facts. If we are to achieve a proper evaluation and perspective of the present status of implantodontics by the resolution of these evidenced inconsistencies, concrete established data should be the firm foundation of the analysis.

In the following six questions and answers, the dental surgeon may find some clarification of the present morass in implantodontics.

I. *Question:* What branches are involved in the application of implantodontics?

Answer: Practically all branches of dental science: anatomy, physiology, histology, pathology, bacteriology, pharmacology, metallurgy, oral surgery, prosthodontics, and roentgenology.

II. *Question:* What are the indications and contraindications for implant dentures?

Answer: A. Indications may be based on either local oral condition or the general condition of the patient.

Local. Any irreversible oral condition which is a hindrance to a successful conventional lower denture, such as: (1) atrophied mandible with a partial or total unilateral or bilateral dehiscent canal, (2) unfavorable position of the mental foramina, (3) extreme atrophy of alveolar ridge with unusual tissue and muscle attachments, (4) extremely sharp mylohyoid ridges, (5) mutilated mouth conditions due to extensive burns or surgery, or (6) macroglossia.

General. Psychologic intolerance to conventional lower denture.

B. Contraindications also may be based on either the local condition of the mouth or the general condition of the patient.

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Local. (1) mouth of recent extractions, (2) presence of natural teeth (especially premolars and molars), (3) impacted teeth or retained roots, (4) cysts or tumors, (5) degenerative bone diseases, or (6) history of poor healing or true kelosis.

General. (1) carcinomatosis, (2) chronic infections (TBC, syphilis, etc.), (3) blood dyscrasias, (4) nutritional disorders (scurvy, osteomalacia), (5) cardiovascular and renal disorders (malignant hypertension, nephritis, etc.), (6) metabolic disorders of bone (osteoporosis, Paget's disease, hyper-hypoparathyroidism), (7) endocrine disorders (Cushing's syndrome, acromegaly, Addison's disease, pituitary insufficiency, etc.), (8) gastrointestinal (bleeding ulcer, cirrhosis of the liver, ulcerative colitis, etc.), (9) general metabolic disorders (diabetes mellitus, etc.). In addition, I feel that the climacteric period could be a possible contraindication in certain cases.

III. *Question:* Why have European dentists encountered such a high percentage of implant failures?

Answer: A. Lack of proper diagnosis of local and general conditions which would spell "failure."

B. Violation of basic surgical principles.

C. Lack of adequate tissue retraction in the first stage for correct surgical impression.

D. Inaccurate impressions and lack of minute details.

E. Short cuts in the two-stage operation.

F. Lack of proper design of the substructure.

G. The use of metals with corrosion properties.

H. Improperly balanced occlusion.

IV. *Question:* Why do American dentists have such a low percentage of failures?

Answer: A. Selectivity of patients.

B. Use of a two-stage operation permitting accurate direct bone impression resulting in a perfectly fitting mandibular substructure.

C. All steps leading to a faultless surgical impression are carefully carried out.

D. Correct design of substructure.

E. Close supervision of patient (postoperative care and dental hygiene).

V. *Question:* What is the ideal method and technique for a mandibular implant?

Answer: There is no ideal method, but there is an accepted technique. The two-stage procedure is an accepted technique. Although this method is

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possibly more traumatic than the one-stage procedure, it is far more accurate. This procedure may vary slightly with the operator, who may incorporate his own modifications.

The following is an outline of an accepted procedure:

At the first appointment intraoral and extraoral (anteroposterior and lateral) roentgenograms and accurate upper and lower impressions are taken. A thorough oral examination is made, and the patient's case history is obtained. The patient is then referred to an internist for a thorough physical examination with special emphasis on bleeding and clotting time and general debilitating diseases.

At the second appointment x-ray films and the internist's report are evaluated.

Centric and vertical positions are established, and the shade and mold of teeth are selected (I prefer plastic teeth with flat cusps).

The third appointment is used for a try-in of the conventional upper and lower setup. The procedure to this point is identical with that of conventional denture construction.

The fourth appointment is devoted to the first stage of the operation. Prior to surgery the patient is given penicillin, 600,000 units intramuscularly, or another antibiotic. Preanesthetic medication consists of 1.5 gr. Nembutal sodium or Seconal sodium, 0.01 gr. atropine sulfate, and 100 mg. Demerol. These agents are administered orally forty-five minutes preoperatively. There are no sure standards for the barbiturates, as many patients react differently to similar dosages. Adjustment in amount must be made with each patient.

Local anesthesia is the anesthesia of choice. A mandibular block and long buccal nerve injection is effected with infiltration anesthesia bilaterally in the anterior portion of the mandible and lingually in the premolar area (because of an accessory innervation by the subcutaneous coli from the cervical plexus).

When anesthesia has been induced, the tissue thickness for the height of the abutment posts is obtained in the cuspid and first molar areas. This is accomplished by inserting the point of a No. 23 explorer through the mucosa to the bone in the above-mentioned four areas and measuring the distance from the tip of the explorer to the small piece of rubber-dam previously slipped onto the explorer which is then recorded for the laboratory.

With a No. 15 Bard-Parker blade, a deep incision through the mucoperiosteum to the bone is made *over the crest of the ridge* from one retromolar pad to the other. At the posterior extension of this incision, accessory incisions are made, forming a "T" with the distal ends of the original incision. These accessory incisions are carried well down over the external oblique and, to a lesser degree, over the mylohyoid ridges. Another accessory incision is made in the midline

of the original incision and well down in the mucolabial fold over the symphysis. These three accessory incisions are made in order to facilitate the obtaining of a good bone impression (Fig. 1).

Starting at the midline and working his way toward the retromolar pad, the surgeon elevates the buccal segment of the mucoperiosteum with a sharp periosteal elevator. Gentle and careful handling of the tissue is necessary as the mucoperiosteum is further elevated. Care must be exercised when the mental foramen area is approached.

Fig. 1.

Fig. 2.

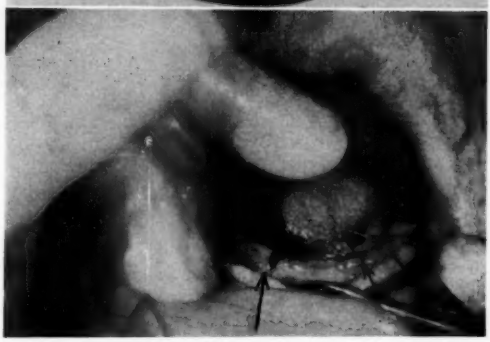

Fig. 1.—Main incision over crest of ridge and the three accessory incisions.
Fig. 2.—Exposed bone with the four grooves.

Then the lingual tissue is retracted. After one side is completed, the operator proceeds to the opposite half. While the tissues are retracted, a clear picture of the anatomy and x-ray findings of the mandible must be kept in mind at all times, especially the position of mental foramen and mandibular canal with possible dehiscence. Spiny ridges must be reduced prior to taking of the surgical impression.

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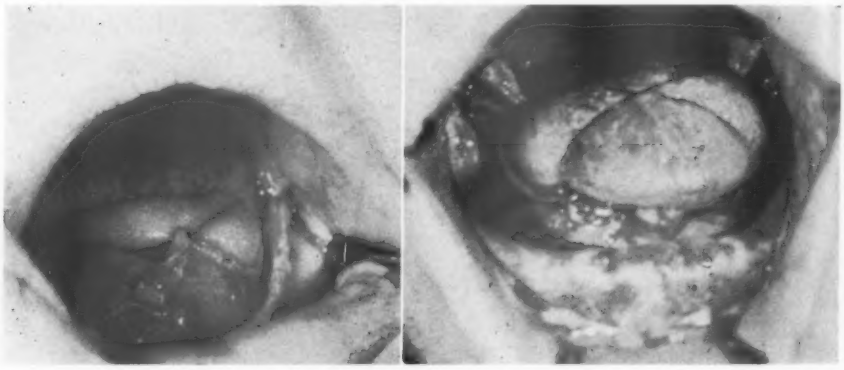
Shallow grooves are made buccolingually with a diamond wheel in the cuspid and first molar abutment areas. These grooves are for easier seating of the substructure. To assure the correct location of the grooves, an "abutment locator" is used (Fig. 2).

The surgical jaw relations are established by inserting the upper denture and the lower cutdown base plate with a bite rim which has been lined with a narrow roll of beeswax. As the patient closes down in proper relationship, the operator obtains the same centric and vertical positions established prior to the first stage of the operation.

The operator is now ready for the surgical impression of the exposed bone, which is taken with previously prepared acrylic resin trays. The lingual flaps of the incision are held away from the bone by a "purse-string" or "shoelace" suture over the tongue (Fig. 3). The buccal flaps are adequately relaxed by the posterior "T" and anterior midline vertical incisions.



A. *B.*

Fig. 3.—*A*, Purse-string type of suture over tongue. *B*, Shoelace type of suture over the tongue.

If a rubber impression material is used, it is best to rim the tray with impression compound. This helps to displace the border tissue, confining the rubber base material. The rubber base material, mixed into a doughy consistency, is then placed in the tray.

During the mixing of the material and the loading of the tray, the soft tissue and bone surface remain covered with gauze packs soaked in hot saline solution to prevent tissue shock by dehydration. At the last minute prior to insertion of the tray, the assistant floods the bone surface with warm saline, removing all clotted blood and debris which might affect the accuracy of the bone impression.

The operator then seats the tray first with a light pressure, retracting the buccal flaps with a blunt instrument and raising the flaps over the tray. When absolutely certain that no tissue is folded under the tray, he then seats it with a steady, firm pressure and holds it firmly for five to seven minutes until it sets to a touch consistency.

After the seal is broken, it is snapped carefully from the bone and examined for shortcomings. If inadequacies are present, the final impression should be repeated.

Fig. 4.

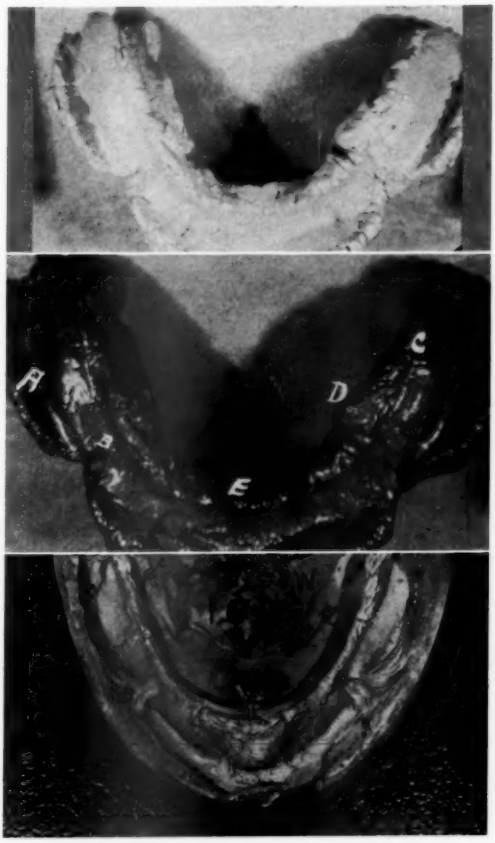


Fig. 5.

Fig. 4.—*Top:* Surgical impression (compound with rubber base).
Bottom: *A*, External oblique ridge; *B*, mental foramen area; *C*, mylohyoid ridge; *D*, dip in premolar area; *E*, genial tubercle area.
Fig. 5.—Master model with some of the landmarks.

Some implantodontists (including myself) prefer to take the impression first with a low-heat compound. Then the impression surface of the compound is slightly relieved and the tray is filled with a zinc oxide impression paste or a rubber base material for the final detailed impression (Fig. 4).

In examining the final impression for detailed accuracy and adequate coverage of landmarks, we look for the following: The

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bone impression should cover the entire bony ridge from one retromolar area to the other. Buccally, it should extend over the crest of the external oblique ridge, the mental foramen area, and the section of labial bone over the symphysis deep down. Lingually, it should cover the mylohyoid ridge, the deep dip of bone in the premolar area, and the genial tubercle area. These areas *must* be included in the surgical impression (Figs. 4 and 5).

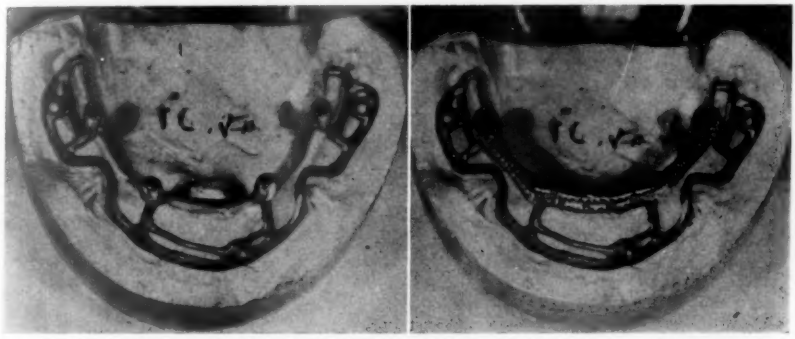
The wound should again be irrigated thoroughly with warm saline and carefully examined for any debris of impression material. Then the area is dusted with Terramycin powder and gently curetted to start fresh bleeding. The edges are carefully approximated and sutured with deeply placed 000 black silk interrupted sutures. An elastic bandage is lightly wound vertically around the chin and horizontally around the forehead and left in place for forty-eight to seventy-two hours.

Instructions should be given as to possible postoperative developments, such as swelling, pain, and difficult deglutition. For pain, a salicylate-narcotic combination, such as aspirin and codeine, Zactirin, or Demerol, is prescribed. Edema and postoperative inflammation are controlled by a neck ice pack and antihistamine drugs. If after forty-eight hours there still is marked edema, trypsin or hyaluronidase (such as "Wydase") may be of value. To combat possible infection, 600,000 units of penicillin or a broad-spectrum antibiotic should be administered intramuscularly once a day for three days, followed by administration of an oral antibiotic for several days. Twenty-four hours postoperatively the patient starts using warm saline mouthwashes to prevent tissue dehydration and to promote healing. To ensure sleep, one of the barbiturates may be prescribed. A high-protein liquid and soft diet is prescribed and supplemented with a multivitamin preparation. Each day when the patient returns for postoperative treatment, the wound should be thoroughly irrigated with warm saline and painted with a 1 per cent solution of acriflavine. About one week later, depending on the healing, the sutures are removed.

As soon as convenient, a stone model of the bone impression is poured following the surgery. After careful separation, the impression should be repoured to furnish a duplicate cast. This is a protection in case of possible loss or damage to one of the models. The implant framework with the position of the four abutments is now designed. The first consideration in the design is the outline of the peripheral border. The most distal extension starts about 3 mm. anterior to the retromolar area and continues buccally beyond the crest of the external oblique ridge. It then continues anteriorly toward the mental foramen area, circumscribing it by about 3 to 4 mm., then downward on the labial plate to the superior aspect of the symphysis. The same outline is carried to the opposite side.

Lingually, from the same distal starting point, the peripheral border of the substructure proceeds anteriorly, avoiding the mylohyoid ridge by about 3 mm. This is very important because of the thinness of the overlying tissue in that area; otherwise, perforation of the tissue may result, with subsequent loss of the implant. In the premolar area the peripheral border of the substructure dips down, taking advantage of the natural undercut generally present in this area. It then proceeds toward the genial tubercles, which it circumscribes superiorly, and continues on the lingual aspect of the opposite side.

Although the screw holes are incorporated in the design, more and more men are getting away from using screws. I have always felt that the use of screws was unnecessary for the fixation of the implant and have emphasized this point in various publications.



A. *B.*

Fig. 6.—*A*, Substructure showing large interspaces, residual ridge practically free of metal, and the peripheral border outline of Vitallium casting.
B, Same as *A* but with superstructure frame.

The two cuspid and two molar abutments are marked on the cast in their respective positions. The position and height of the abutments are determined by the amount of intramaxillary space. They should be placed over the center of the crest of the ridge if possible. The height of the four abutment posts is governed by the thickness of the mucoperiosteum as established with the explorer. Some men today design the abutments without posts.

The case should be designed in such a way as to allow for as many interspaces as possible (but not at the expense of weakening the implant) and, most important of all, to have as little metal as possible over the residual ridge in order to permit a greater area of tissue contact with the bone where the incision was made and also greater tissue proliferation through the interspaces, thus firmly anchoring the implant by periosteal fibers which reattach themselves to the cortical bone through the meshwork of the implant (Fig. 6).

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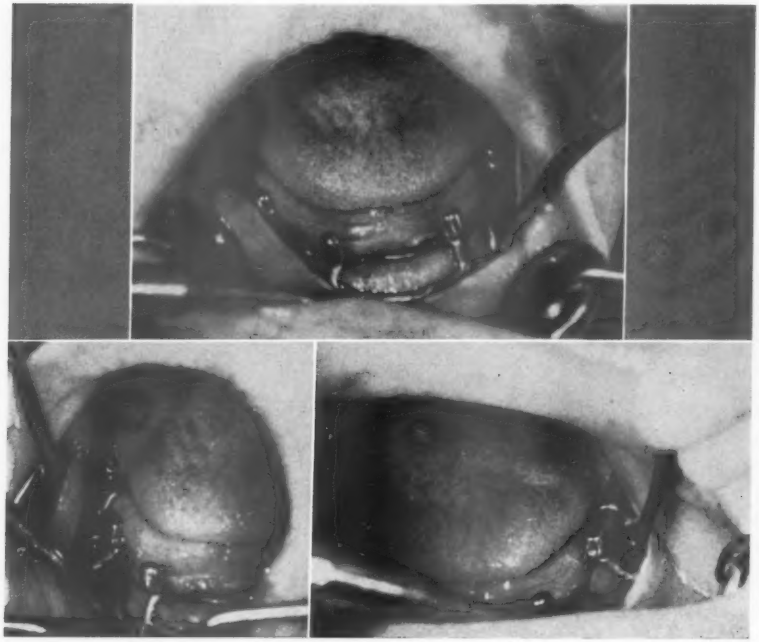
The fifth appointment is devoted to the second stage of the operation. About one month after the first stage of the operation (depending on the healing), the implant is inserted. Premedication and anesthesia are the same as for the first stage. The incision differs from the one in the first stage. Only the main incision is required; the accessory incisions are not necessary. The incision is

A.



B. *C.*

Fig. 7.—*A*, Implant seated showing accurate fit. *B*, Right side. *C*, Left side.

started at one retromolar area down to the bone through the mucoperiosteum and carried along the crest of the ridge, following the original line of incision, to the opposite side. The retraction of the mucoperiosteum is accomplished without any difficulty, since the periosteal fibers did not have sufficient time to reattach themselves to the cortical bone. The insertion of the implant does not call for extensive retraction of the mucoperiosteum as did the bone impression; nevertheless, it should be sufficient to encompass the depth of the implant and to allow easy seating and thorough checking of the accuracy of the implant fit on the bone. There should be no space between the meal and the bone (Fig. 7).

To seat the substructure correctly without any danger of possible bending of the casting, it is wise to place the superstructure unto

the four abutments. The downward pressure on the superstructure will assist the substructure in better seating without the danger of damaging the substructure. If advantage has been taken of all the natural undercuts (provided they were clearly incorporated in the surgical impression), the casting will usually snap into place when seated.

It is understood that the substructure prior to the second stage of the operation was autoclaved. The substructure is sandblasted and not polished. Only the abutments are polished.

Before final closing, the wound is thoroughly irrigated with warm saline, and the bone and implant are dusted with Terramycin powder. The free mucoperiosteal flaps are then curetted gently to start fresh bleeding.

The wound edges are carefully approximated and closed with black silk 000 sutures. Deep vertical mattress sutures are placed around each abutment post, tightly but without blanching the tissues. This type of suture will usually avoid inversion of the free tissue ends and is more favorable for healing by primary intention. Between the two cuspid abutments a deep horizontal mattress suture is placed. Interrupted sutures are placed about 1 cm. apart at one end of the incision all the way to the opposite side.

As soon as the suturing is completed, the entire area of incision is covered with hot saline compresses for ten to fifteen minutes. This will restore the tissues to their normal color. X-ray films are then taken.

An immediate temporary acrylic superstructure or splint, occluding with the patient's old upper denture, is inserted and an elastic chin-head bandage is applied (see first stage of operation). The splint protects the mucosa and stabilizes the implant during the period of fibrous attachment. This acrylic splint in the form of a full lower bite rim fits over the four abutments and is not tissue-borne. It usually has the six anterior teeth only for improved esthetics. In the posterior region, the acrylic is built up on a flat plane in order to eliminate lateral displacing forces (Fig. 8).

Postoperative care is exactly the same as after the first stage of the operation described previously.

Approximately four to six weeks after the second stage of the operation, the patient returns for the completion of the prosthetic phase of the implant denture.

The abutments are lined with petrolatum and the superstructure is seated. This facilitates the removal of the superstructure with the alginate impression material in the pick-up impression. The model is poured in hard stone. Then a wax bite rim is adapted to the frame of the superstructure and contoured to meet the model beneath it. Centric and vertical positions are then obtained. The setup is completed for the try-in.

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If the operator is satisfied with the functional and esthetic requirements, the case can then be completed (Fig. 9). The processing of the acrylic material must be done with the utmost care so that only a minimum amount of shrinkage occurs. Otherwise, the superstructure will act as an orthodontic appliance due to the distortion of the superstructure frame.

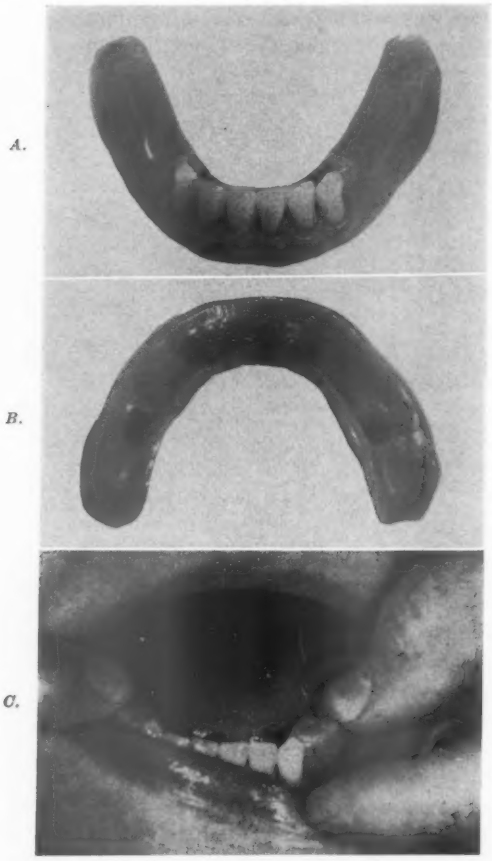
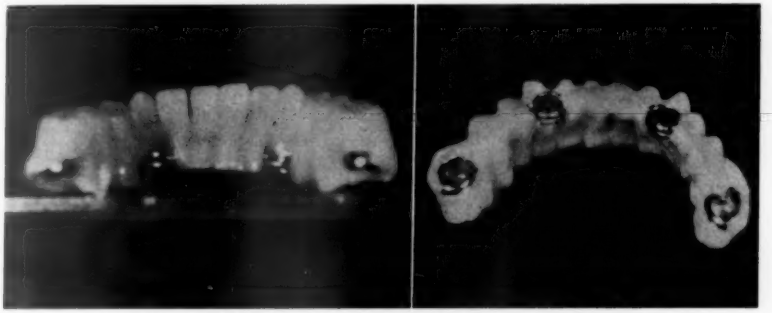


Fig. 8.—*A*, Acrylic immediate superstructure (splint) with six anterior teeth.
B, Inside of splint with the four openings which seat over the four abutments of the superstructure.
C, Splint seated over the four abutments of the substructure.

Once the completed dentures are inserted, the occlusion must be carefully checked in centric, protrusive, and lateral excursions. A perfect balanced occlusion is of utmost importance since the forces of occlusion are transferred directly to the bone. Also the denture cannot be tissue-bearing; this will interfere with proper circulation.

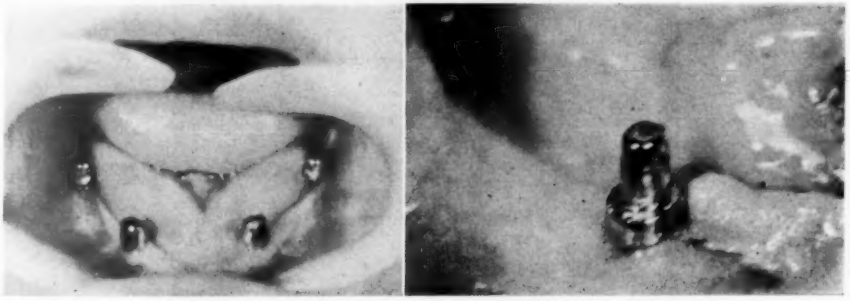
VI. *Question:* What is the percentage of successful full lower implants?

Answer: Relying on communications from colleagues with up to ten years' experience with implants, we know that with the two-stage operation, approximately 95 per cent of mandibular implants have given comfort, function, and happiness to patients with difficult and hopeless denture problems. A case is successful when there is (1) absence of pain, (2) absence of pathology, clinically and roentgenographically (Figs. 10 and 11), and (3) comfort, function, and stability.



A. *B.*

Fig. 9.—Superstructure completed with teeth. *A*, Lingual view. *B*, Undersurface showing neck of teeth without artificial gum tissue.



A. *B.*

Fig. 10.—*A*, Healing of tissue around abutments. *B*, Close-up of one abutment.

SUMMARY AND CONCLUSIONS

The problem of indications and contraindications for implant dentures and the careful selection of patients has been presented.

Mastering the technique and recognizing the factors that spell contraindication are of utmost importance, but a thorough understanding of bone and its overlying tissues is of equal importance. Osler expressed this basic principle in his memorable statement: "A man's practice is as his knowledge of pathology."

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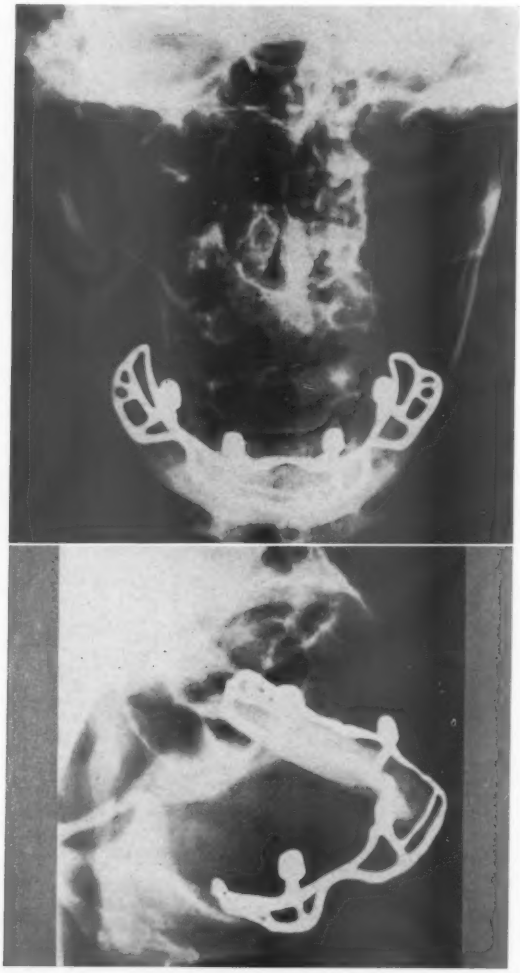
Instead of blaming implants per se for their failures, I wish to place responsibility on the operator for improper judgment and incorrect techniques.

With the development of the two-stage operation and meshwork design, we are able to obtain an accurate direct surgical impression that enables the operator to cast a perfectly fitting mandibular substructure. When metal over the crest of the ridge is eliminated the wound edges will be directly over

A



B.

Fig. 11.—X-ray films of substructure twelve months after operation. *A*, Anteroposterior view. *B*, Lateral view.

bone, facilitating the reattachment of the periosteum to the bone and healing by primary intention. The meshwork design invites larger contact areas between periosteum and bone, thus anchoring the implant to the bone. The material of the implant should be nonelectrolytic and chemically inert in its relationship with the surrounding hard and soft tissues and should be noncorrosive.

If the operator adheres to all the principles as outlined, the percentage of failure should be practically nil.

While there are some questions yet to be answered, there is no indication that they are insurmountable.

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EXODONTIA

THE INEFFECTIVENESS OF CARBAZOCHROME SALICYLATE (ADRENOSEM) IN THE REDUCTION OF SURGICAL BLEEDING

Robert J. Gores, D.D.S., Rochester, Minn.

CARBAZOCHROME salicylate (Adrenosem salicylate) is a systemically administered agent which is said to be useful in reducing the loss of blood during surgical procedures. Much has been written in support of the usefulness of this drug, not only in reducing the amount of blood lost during surgical procedures, particularly in the field of oral surgery, but also in promoting more rapid healing of wounds and in reducing postoperative bleeding and morbidity.[1-5]

To my knowledge, none of the authors of the published reports dealing with the use of carbazochrome salicylate measured quantitatively, by an accurate method, the blood lost during surgical procedures in a series of cases in which the drug was used and in a suitable control group. Some skepticism, however, was expressed concerning these claims in an American Medical Association report on this drug[6] and in an article by Marcus and Spaet,[7] who used the drug in a double-blind study in thoracic surgery. The latter report stated that clinical observations cannot be regarded as a reliable method of evaluating a drug and that Adrenosem probably is of no value as a systemic hemostatic agent.

It is well known by all who have studied the surgical loss of blood that visual estimates of the quantity of blood lost during an operation are totally unreliable, even when the estimates are made by experienced surgeons.[8-11]

Therefore, this study was undertaken to determine the effectiveness of Adrenosem salicylate in the reduction of the blood lost during multiple extractions and alveoloplasty. The blood lost was measured quantitatively by an accurate method.

PRELIMINARY STUDIES

Prior to clinical trial, the effect of Adrenosem salicylate on the capillaries and small vessels was observed through a Clark window inserted in the ear

From the Section of Dentistry and Oral Surgery, Mayo Clinic and Mayo Foundation.
The Mayo Foundation, Rochester, Minnesota, is a part of the Graduate School of the University of Minnesota.

of a rabbit.[12] The vascular bed under the window was observed through the microscope while solutions of Adrenosem salicylate, normal saline, and 1:10,000 epinephrine hydrochloride were injected into the vessel leading to the capillary bed in the window.

The injections were made by one person while another observed the changes in the vessels. The person observing the vascular bed through the window did not know which drug was being injected or precisely when it was injected. No change in the vascular bed, either in size of the lumen or in rate of blood flow, could be observed when the normal saline and Adrenosem solutions were injected. In contrast, marked contraction of the vessels and reduced rate of blood flow were observed almost immediately when the solution of epinephrine hydrochloride was injected.

This procedure was carried out because it is known that much of the bleeding that occurs during multiple extractions and alveoloplasty comes from small vessels and capillaries, and it is reasonable to assume that any drug that would be effective in reducing capillary and small-vessel bleeding also would have to affect these vessels either by constricting them or by reducing blood flow through them in some other way.

METHOD AND PROCEDURE

A total of fifty-three patients were studied. Twenty-seven served as controls, and twenty-six were given Adrenosem salicylate before operation.

No criterion was employed in the selection of the patients for this study except that they were all candidates for multiple extraction and alveoloplasty that involved one or both dental arches. Some of the patients, in addition to the erupted teeth, had impacted teeth, root end abscesses, retained dental roots, and tori which also were removed surgically.

The alveoloplasty procedure was graded by the surgeon and his assistant from 1 to 4 after a method which Royer, Mann, and I[13] described in 1955, as follows: Grade 1 indicates removal of teeth without cutting of alveolar bone or producing alveolar mucoperiosteal flaps; grade 2 involves removal of teeth and removal of interproximal bone from alveolar crests, without extensive mucoperiosteal flaps; grade 3 includes removal of teeth with moderate removal of alveolar bone from crests and from buccal or labial aspects (either or both) and extensive mucoperiosteal flaps; and grade 4 indicates removal of teeth and extensive removal of alveolar bone from crests and from buccal or labial aspects (either or both), with extensive mucoperiosteal flaps.

The operations were performed by four different surgeons, who used essentially the same surgical technique and procedure. A general anesthetic was used in all instances, and the preanesthetic medication consisting of 1 to 2 mg. levorphanol tartrate (Levo-Dromoran), 1 mg. levallorphan tartrate (Lorfan), 1/150 grain atropine sulfate, and 25 mg. promethazine hydrochloride (Phenergan) was standard. Anesthesia was produced by use of thiopental sodium in 2.5 per cent solution, administered by the intravenous fractional method. In all instances the anesthesia thus produced was augmented with nitrous oxide and oxygen administered through a nasal intratracheal tube.

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Of the fifty-three patients studied, twenty-six were prepared preoperatively with carbazochrome salicylate (Adrenosem salicylate). Each of these twenty-six patients received 5 mg. of Adrenosem salicylate intramuscularly one and one-half to two hours prior to the beginning of the operation. Most of the Adrenosem-treated patients complained of mild burning when the Adrenosem salicylate was administered, but otherwise they sustained no noticeable side effects from the drug.

The remaining twenty-seven patients served as a control group. Except for the omission of Adrenosem salicylate, their preoperative preparation was identical to that of the first group.

All blood lost during surgery was saved. Most of the blood was recovered by aspirator, and the remainder was recovered in gauze sponges and in the oropharyngeal throat pack. After operation, the instruments and gloves were wiped free of blood with wet sponges. All sponges and the oropharyngeal pack were saved and covered with water immediately after the operation.

The blood lost at operation was measured by a method previously described,[13] which is essentially the same as a method used by Pilcher and Sheard[14] in 1937. The method is based on the determination of the quantity of hemoglobin in the blood lost during operation. When the exact quantity of hemoglobin lost during operation and the concentration of hemoglobin in the patient's blood immediately before operation in grams per 100 c.c. of circulating blood are known, it becomes a simple arithmetic procedure to determine the total blood lost at operation by applying the following formula:

$$\frac{\text{Total grams of hemoglobin in lost blood}}{\text{Grams of hemoglobin per 100 c.c. in patient's blood before operation}} \times 100 = \text{c.c. of blood lost}$$

The accuracy of this method of determining blood lost during surgical procedures has been confirmed by Wilcox,[15] who measured blood lost during cesarean section in 1957 at the Mayo Clinic, with an error of about 1 per cent.

RESULTS

Patients undergoing alveoloplasty of grades 1 and 2 were grouped together; on most of the patients in this group grade 2 alveoloplasty was performed. Likewise, patients having alveoloplasty of grades 3 and 4 were grouped together; on most of the patients in this group an alveoloplasty of grade 3 was performed.

The largest quantity of blood lost by any patient in this study was 1,199 c.c. This rather large blood loss occurred in the Adrenosem salicylate group, but the case was not one of the twenty-six included in the series, since the patient had extensive periodontal disease which was accompanied by a great deal of gingival inflammatory reaction and there was no comparable case of extensive periodontal disease in the control group. One patient in the series of fifty-three lost 768 c.c., and another lost 752 c.c., but the remainder lost less than 700 c.c. of blood.

In the group of twenty-six patients treated with Adrenosem salicylate, the average loss of blood was 358 c.c. In the subgroup of alveoloplasty, grades 1 and 2, the average loss of blood was 234 c.c., and in the subgroup of alveoloplasty, grades 3 and 4, the average loss was 465 c.c.

In the control group of twenty-seven patients, the average loss of blood was 353 c.c. In the subgroups of alveoloplasty, grades 1 and 2, and alveoloplasty, grades 3 and 4, the average blood losses were 220 and 476 c.c., respectively.

In comparing the blood lost in the group treated with Adrenosem and the control group (Fig. 1), one is not impressed with any reduction in loss in the group treated with Adrenosem. The average blood lost in the two groups was very similar.

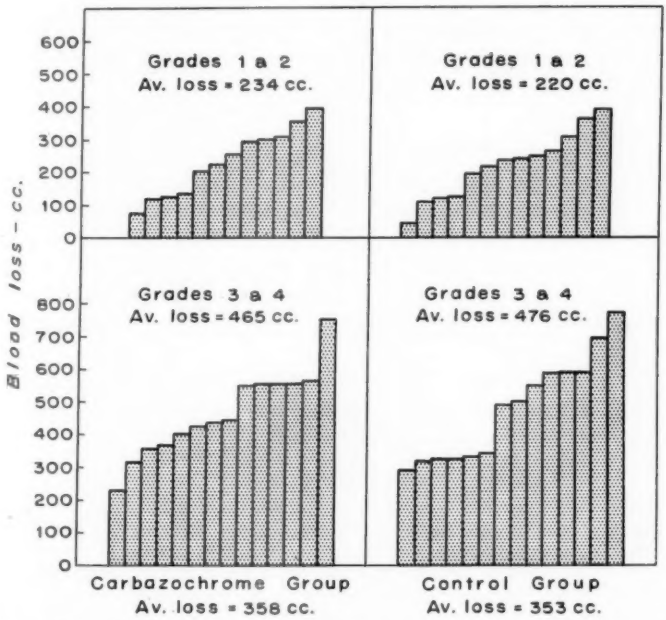

Fig. 1.—The ineffectiveness of carbazochrome salicylate in the reduction of bleeding at oral operations consisting of multiple extractions and alveoloplasty. Loss of blood by twenty-six patients treated with carbazochrome salicylate before operation and by twenty-seven patients in the control group is shown.

COMMENT

In a series of forty-seven cases reported on in 1955,[13] it was found that the average loss of blood per operation for multiple extraction and alveoloplasty was about 340 c.c.; however, in one instance as much as 771 c.c. was lost. Johnson[11] also measured blood lost during similar surgical procedures and confirmed these results. Middleton,[16] studying loss of blood during oral surgical procedures in 1957, again confirmed these results and, in addition, measured

loss of blood during the immediate postoperative period and found that the postoperative loss of blood almost equaled the loss at operation in many instances.

None of the fifty-three patients in my present series was given fluids or transfusions of whole blood before, during, or after operation. All patients left the hospital on the day following operation. No abnormal postoperative bleeding occurred in any case, and healing was uneventful in all cases.

When operation for removal of teeth and alveoloplasty is performed in the manner described, without the use of a local anesthetic containing a vasoconstrictor drug infiltrated into the soft tissue adjacent to the operative field, use of carbazochrome salicylate apparently is of little value in reducing the loss of blood at operation.

Middleton[16] and I[13] have shown that use of local anesthetics containing a small quantity of vasoconstricting drug infiltrated locally into the soft tissue adjacent to the operative field will reduce the surgical loss of blood as much as 50 per cent in the average patient.

SUMMARY

The loss of blood was measured in fifty-three patients who underwent multiple extractions and alveoloplasty under general anesthesia. No local anesthetic was employed in any case. Of the fifty-three patients, twenty-six were prepared preoperatively by the intramuscular injection of 5 mg. of carbazochrome (Adrenosem) salicylate one and one-half to two hours prior to the operation. The remaining twenty-seven patients served as a control group.

When operations of equal extent and severity were compared, it was found that no effective benefit in reduction of loss of blood at operation was noted in the patients treated with carbazochrome salicylate.

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PERIODONTICS

OBSERVATION ON SOME GENETIC CHARACTERISTICS OF THE PERIODONTIUM IN THREE STRAINS OF INBRED MICE

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INTRODUCTION

THE effects of both dietary deficiencies and physical consistencies of diets on the jaws and periodontium of various laboratory animals have been reported upon rather extensively. A search of the literature, however, revealed only one investigation dealing with strain differences of laboratory animals on diets of similar physical consistency and nutrient quality. This was a histologic investigation of age changes in the periodontium of molar teeth in the Norwegian and albino rats, both fed a dog chow pellet diet. The main differences noted between these two strains were that the Norwegian rat showed greater interproximal attrition, whereas the albino rat showed a greater cementoblastic, activity.

It was the purpose of this investigation, therefore, to study the strain difference of inbred mice on similar dietary regimes.

MATERIALS AND METHODS

Inbred male mice, 30 days of age, of strains DBA/2JN, C57L/HeN, and STR/N were used. They were maintained on four different diets. Diet 1, Purina Laboratory Chow, was of a hard physical consistency and will be referred to as stock diet. Diet 2, a high-fat diet of a soft, greasy consistency, will be referred to as diet 10046, and it has the following formula*:

Casein (vitamin-free)	25%	Vitamin powder #307	1%
Fat (Crisco)	57%	Liver powder	5%
Sucrose	2.75%	Methionine	0.25%
Salts (HMW)	6%	B_{12} solution 20 mcg./ml.	1 ml.
A and D oil #1†	2%	Niacin solution 2 mg./ml.	2 ml.
E oil #1‡	1%	Aureomycin	50 mg.%

*This diet was developed by Dr. Olaf Mickelsen, National Institutes of Health.

†Wesson oil containing 0.5 per cent Natola (secured from Parke-Davis, Inc.). The Natola provides 550 I.U. vitamin A and 110 I.U. vitamin D per 100 Gm. diet.

‡Wesson oil containing 5 mg. α-tocopherol acetate per 100 Gm. diet.

Diet 3 was a high-fat diet with a cellulose filler, of a soft, powdery consistency. It will be referred to as diet 10046A, and it consists of the following:

Diet 10046	62.4%
Solka Floc (cellulose filler)	37.6%

Diet 4 was a nutritious diet of a watery consistency. Its formula is as follows[7]:

Cellu flour	6%
Wesson salt mixture	2%
Diet yeast (Pabst)	0.5%
Cod-liver oil	0.5%
Vitamin K	5 mg.%
Mazola oil	10%
Casein (crude)	8%
Wheat germ oil	0.5%
Starch	10%
Dextrin	9.5%
Sucrose	10%
Water	43%

This diet will be referred to as diet 10005A or Ingle's diet.

The three strains were divided into four groups, each of which was placed on one of the above four diets. The animals were housed in plastic cages in groups of one to five (usually four) and maintained on the experimental diets for fifteen months. At 16 months of age, the mice were killed with ether; the heads were removed and fixed in 10 per cent formalin. The heads of seventy-two animals, six from each group of the three strains, were arbitrarily selected for histologic study, and the remainder were defleshed.

The heads of the animals selected for histologic investigation were decalcified in 5 per cent formic acid, split in a midsagittal plane, dehydrated in ethanols, embedded in paraffin, and sectioned serially at 6 microns. The tissues were sectioned in a mesiodistal direction, and the sections were stained with hematoxylin and eosin.

The remaining heads were autoclaved to permit gross removal of flesh, then incubated at 37° C. for five days in an aqueous solution of papain, bleached in Superoxol, and then placed in acetone for removal of fats and remaining debris. The tissues were allowed to dry in air overnight before the following observations and measurements were made: (1) maxillary width, (2) mandibular weights, (3) the presence and degree of periodontal involvement, and (4) wear patterns on the occlusal surfaces of the molar teeth.

The histologic material was used to describe (1) the general nature of the periodontal lesion found and (2) the trabecular pattern of the alveolar bone.

The scope of this investigation was limited somewhat because of an extremely high mortality rate in strain C57L/HeN on diet 10005A.

Methods of Scoring.—

Maxillary width: This was measured with a micrometer caliper from the buccal surface of the first molar on one side to the buccal surface of the first molar on the opposite side. It was not possible to make this measurement in strain STR/N because of the marked mobility of the molar teeth.

Mandibular weights: The lower jaws were weighted on an analytical balance and the weights were recorded in milligrams.

The presence of periodontal disease (alveolar bone resorption): These observations were limited to the maxillary and mandibular teeth on one side of the defleshed specimens. A numerical system of scoring the lesion, a modification of that described by Gupta and Shaw,[2] was used. The classification is as follows:

0 = No detectable bone resorption.
1 = Slight alveolar bone resorption with one fourth or less of the root exposed.
2 = Moderate bone loss with one fourth to one half of the root exposed.
3 = Moderately extensive bone loss with between one half and three fourths of the root visible.
4 = Severe bone loss with more than three fourths of the root showing.

The area of greatest bone loss, whether buccal, lingual, mesial, or distal, is used for the numerical classification of the entire tooth. Each tooth, therefore, has but one numerical designation.

Wear patterns: Wear was classified into two categories:

(a) "No" wear = No detectable wear or very slight wear with no cusp obliteration.
(b) "Pronounced" wear = Obliteration of at least one cusp with underlying dentine showing through.

RESULTS

Although the experiment was designed primarily to study strain differences on the same and different diets, little additional effort was required to verify the diet differences in the same and different strains.

Mandible Weights.—The mandibular weights of strain C57L/HeN were in all cases greater than those of strain DBA/2JN (Table I). Regardless of the strain, however, the type of diet did have an effect on the weight of the mandible. In all three strains, the animals on the high-fat diet had heavier mandibles than those on stock diets.

The effects of the diets within the strain were as follows:

In strain C57L/HeN the average mandibular weight of the animals on stock diets was 90.3 mg., while the weight of those on diet 10046 was 98.1 mg. This difference is statistically significant at the probability level of 1 per cent.

In strain DBA/2JN the average weight of the mandibles for the animals on stock diet was 72.6, and for the animals on diet 10046 it was 77.7 mg. This comparison does not yield a statistical difference.

In strain STR/N the average weight of the mandible for the animals on stock diet was 86.0 whereas for those on diet 10046 it was 93.8. This difference is significant.

TABLE I. AVERAGE WEIGHT OF MANDIBLE (MG.) BY STRAIN AND DIET

STRAIN	DIET		
	STOCK	10046A	10046
C57L/HeN	90.3	94.5	98.1
DBA/2JN	72.6	77.0	77.7
STR/N	86.0	87.2	93.8

Maxillary Width.—It will be noticed in Table II that on stock diet strain C57L/HeN has an average width of 0.179 inches and the corresponding DBA/2JN width is 0.171. Thus, strain C57L/HeN has, on the average, a greater maxillary width than strain DBA/2JN on stock diet. In the remaining two diets, however, it is evident that strain DBA/2JN has, on the average, a greater maxillary width than strain C57L/HeN. Thus, the comparison of the strain averages contains a reversal of size, depending on the diet consumed.

The effects of the diets within the individual strain were as follows:

In strain C57L/HeN the average width of the maxilla for animals on stock diet is the same as for the animals on diet 10046.

In strain DBA/2JN the average width of the maxillas for the animals on stock diet was 0.171, while the corresponding average for the animals on diet 10046 was 0.180. This difference is highly significant.

Table II summarizes the maxilla width data by giving the average maxilla width, in inches, for the sixty animals by strain and diet.

TABLE II. AVERAGE MAXILLA WIDTH (INCHES) BY STRAIN AND DIET

STRAIN	DIET		
	STOCK	10046A	10046
C57L	0.1789	0.1781	0.1791
DBA	0.1708	0.1794	0.1803

Periodontal Disease (Alveolar Bone Resorption).—Table III summarizes the number of animals in each strain on each diet and gives the corresponding average *total* score for the maxilla and mandible. The three scores for each animal were totaled, and the average total score was obtained by dividing the sum of the total scores by the number of animals involved.

It seems apparent that the conclusions concerning strain and diet differences are the same, whether the maxillary or the mandibular periodontal score is used. It also seems apparent that strain STR/N is susceptible to periodontal disease, whereas strains DBA/2JN and C57L/HeN are resistant. Since the

TABLE III. NUMBER OF ANIMALS AND AVERAGE TOTAL PERIODONTAL SCORES FOR MAXILLA AND MANDIBLE BY STRAIN AND DIET

DIET		STRAIN					
		STR/N		C57L		DBA	
		Maxilla	Mandible	Maxilla	Mandible	Maxilla	Mandible
Stock	No. of animals	10		10		10	
	Average	9.4	10.3	1.9	1.7	2.2	1.5
10046	No. of animals	10		10		10	
	Average	11.0	11.6	0.7	2.5	0.0	0.9
10046A	No. of animals	9		15		11	
	Average	10.0	11.0	0.5	1.0	0.0	1.0
Ingle	No. of animals	10				10	
	Average	4.6	8.0			0.3	0.5

maximum score per animal is 12, an average score of 11 or more must of necessity come from a group whose individual numbers have a total score close to the maximum; hence, the variability of the total scores is small. As a matter of fact, the lowest total periodontal score for strain STR/N on diet 10046A was 7 for the maxilla and 11 for the mandible. The average total scores for strains DBA/2JN and C57L/HeN are quite small. No maxilla total score exceeded 3 for strain C57L/HeN on either diet 10046 or 10046A. Each of the twenty-one DBA/2JN animals on diets 10046 and 10046A had a maxilla total score of 0. The largest mandible total score was 7, for one animal of strain C57L/HeN on diet 10046. Two other animals had total mandible scores of 4. Considering these wide differences, then, the assertion that it is apparent that a strain difference exists is valid. (Figs. 1 and 2 illustrate these differences.)

TABLE IV. ANALYSIS OF VARIANCE (SQUARE ROOT OF SCORES) STRAIN STR/N

SOURCE	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F
Maxilla				
Mean	1	327.4103		
Total	38	12.5897		
Diets	3	8.8873	2.9624	28.00 (significant)
Within diets	35	3.7024	0.1058	
Mandible				
Mean	1	394.2564		
Total	38	3.7436		
Diets	3	2.0165	0.6721	13.63 (significant)
Within diets	35	1.7271	0.0493	

The diet comparison of periodontal disease scores for strain STR/N required a statistical analysis based on the square root of the scores. This yielded a highly significant difference between diets, for strain STR/N, in terms of the square root of the maxilla periodontal scores (Table IV). The same conclusions, but at a lower probability level, can be drawn about diet differences in terms of the mandible score.

Wear on the Occlusal Surfaces of the Molar Teeth.—In strain C57L/HeN on diet 10046A, eight out of a total of fifteen mice showed pronounced wear (Fig. 3). Wear was not present in mice on any other diet or in any other strain.

Fig. 1.—An example of the severe alveolar bone loss found about the molar teeth of an STR/N male mouse, 16 months of age, on a high-fat diet (diet 10046).

Fig. 2.—A DBA/2JN male mouse, 16 months of age, on a high-fat diet (diet 10046), demonstrating the relatively normal height of the alveolar bone present in this strain of mouse.

Histologic Observations.—

Trabecular pattern: The trabecular patterns of the alveolar bone were specific for each strain and were not altered by the diet consumed. Strain

C57L/HeN has a fine trabecular pattern to its alveolar bone; strain DBA/2JN has a course type of trabeculation. Strain STR/N has also a course trabecular pattern but, in addition, has prominent cement lines running throughout.

The periodontal tissues: The histologic sections confirmed the gross findings made on the defleshed specimens.

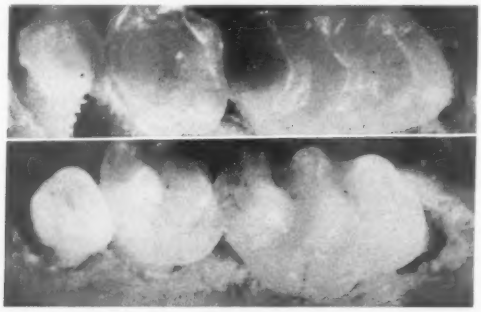

Fig. 3.—*Top:* Wear patterns on the occlusal surfaces of molar teeth of a C57L/HeN mouse on diet 10046A, which is of a soft, powdery consistency. *Bottom:* Lack of occlusal wear on the molars of a C57L/HeN mouse on a stock diet, which is of a hard physical consistency.

Fig. 4.—A mesiodistal section through the molar region of a C57L/HeN mouse on diet 10046, illustrating a normal periodontium.

Strains C57L/HeN and DBA/2JN have, in general, healthy-looking periodontal structures, regardless of the diet. Fig. 4 shows mesiodistal section through the first and second maxillary molar region demonstrating the normal interproximal tissue configuration.

Fig. 5, on the other hand, illustrates the type of configuration found in the interproximal area of the maxillary molar region in strain STR/N on diet

10046 or 10046A. Extensive pocket formation with severe loss of alveolar bone can be seen. These peridontal pockets are not associated with the presence of calculus, and hair impaction is rare.

On diet 10005, however, a much milder type of periodontal involvement occurs in strain STR/N.

Although not enough animals of strain C57L/HeN on diet 10005A survived to be included in this study, the few animals studied seemed to indicate that they followed the typical characteristics of their strain in regard to resistance to periodontal disease.

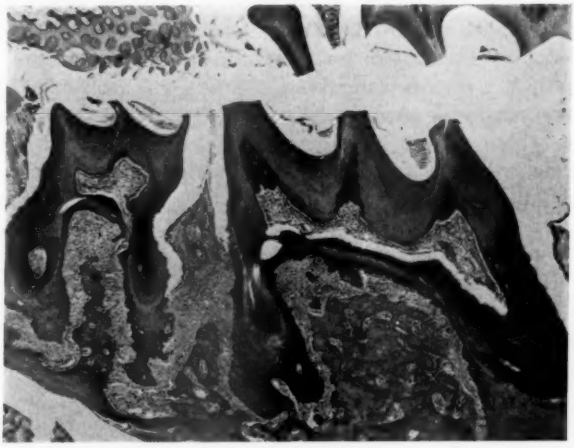

Fig. 5.—A mesiodistal section through the molar region of a STR/N mouse, demonstrating a typical periodontal pocket found interproximally in this strain on diet 10046.

DISCUSSION

It has been postulated that an important predisposing cause of periodontal disease is frail development of the supporting structures.[3] The experimental work to substantiate this was done in the rat by Watt and Williams.[4] Both adult and weanling rats were divided into two groups. The diets fed to each group were identical in chemical composition but differed in that the physical character of one was hard while that of the other was soft. At the end of four months the animals of both groups which had consumed the hard diet had mandibles that were heavier and greater in bulk than those fed a soft, pappy diet. The results concerning the width of the maxilla, however, were somewhat different. The young animals on the hard diet showed an increase in the width of their maxillas, while in the adult animals no effect was noticed. No evidence was presented by these authors, however, to prove that a heavier and more bulky jawbone was more resistant to periodontal disease.

Our experiment differed from that of Watt and Williams in several aspects. First, there was a species difference. Second, there was a strain difference. Third, the diets varied in nutrient quality as well as physical consistency. The

results we obtained indicated that the physical character of the diet per se was not the sole or necessarily the most important determining factor in producing increased maxillary widths or mandibular weights. In fact, in all three strains the animals fed a high-fat diet of a soft physical consistency had heavier mandibles than those on a stock diet of a hard physical consistency. One cannot conclude from these facts, however, that the alveolar process alone was responsible for the increased weight of the mandible. The data merely indicate that the entire mandible of the animals on the high-fat diet is heavier. Furthermore, neither hard nor soft physical consistency of the diet appeared to be of importance in making the animal more resistant to periodontal disease. The strain of animal alone was the factor of prime importance in determining its susceptibility or resistance to periodontal breakdown. An interesting finding was that the periodontal disease was less severe in strain STR/N mice which consumed diet 10005A, a diet of watery consistency. The reason for this increased resistance may possibly be explained by the fact that all the animals of strain STR/N, except those on diet 10005A, spontaneously develop a hydronephrosis.

The statement that wear on the occlusal surfaces of teeth is a result of the hardness of the diet,[5] although undoubtedly true for certain species and certain strains, is not necessarily a true generalization. We were able to find pronounced wear on the occlusal surfaces of the molar teeth only in those animals of the C57L/HeN strain which consumed diet 10046A, a soft, powdery diet. Recently, Estrada[5] reported some findings of interest in the Katia Indians. He observed marked wear of the teeth in the Katia Indians, even though the diets which these Indians consumed were soft. No explanation for these phenomena was given. The explanation may well be, however, that the hardness of the diet is not so important as the abrasive properties of the individual components which are responsible for marked occlusal wear. Many primitive tribes consume large quantities of sand with their food, while the C57L/HeN mice on diet 10046A consumed large quantities of cellulose in theirs. The fact, however, that the molar teeth in strains DBA/2JN and STR/N on this very same diet were unaffected demonstrates once more the importance of strain differences. Neither we nor other investigators, however, have been able to demonstrate that pronounced wear is protective or, conversely, that absence of marked occlusal wear is an etiological factor in periodontal disease.

The general configuration of the periodontal pocket observed in the histologic material in strain STR/N on diet 10046 and diet 10046A, was extremely similar to that found in the human being and would indicate that this strain of mouse is a valuable animal for periodontal research.

The marked difference in the occurrence of periodontal lesions in three strains of mice demonstrates the fact that one must exercise caution in evaluating experimental variables.

SUMMARY AND CONCLUSIONS

1. Under the conditions of this experiment, strain STR/N is susceptible to periodontal disease, while strains DBA/2JN and C57L/HeN are relatively resistant to periodontal disease.

2. In strain DBA/2JN the maxillas of the animals on the high-fat and high-fat-plus-filler diets are wider than those on stock diet.

3. In all strains the mandibles of the animals on the high-fat and high-fat-plus-filler diets weigh more than those of animals on stock diet.

4. Neither the physical consistency of the diet, the width of the maxilla, nor the weight of the mandible is an important etiological factor in periodontal disease in these strains of mice.

5. The trabecular pattern of the alveolar bone is distinct for each strain. Regardless of the nature of the diet, these patterns remained unchanged.

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ORAL MEDICINE

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DIET, NUTRITION, AND DENTISTRY

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DENTAL disease is so widespread that about 95 of every 100 persons are affected. At present, only about 35 per cent of these receive adequate but not optimum care. This lag between the incidence of the disease and adequate care will be more serious in our rapidly growing population unless there is a corresponding increase in dental facilities together with a greater interest in preventive measures for an expected population of 228,000,000 in 1975.[1]

The severity of the problem was illustrated by World War II draftee rejections.[2] Of the first 2,000,000 draftees examined, figures showed that the highest percentage of rejections were attributable to the inability of the young men to meet the minimum dental requirement of possessing nine teeth in occlusion.

The real solution would be the prevention of dental disease, based on the understanding of both hereditary and environmental factors responsible for the formation of good teeth and sound supporting tissues. To meet the challenge, there has been in recent years a great expansion in research activity supported by government and private agencies, but more is needed.

There is distinct evidence that nutrition of the embryo[3,4] as well as that of the growing young, will affect dental health.[5-7] However, further study is required to determine exactly what is optimum nutrition for the development of good teeth and sound supporting tissues. A specific nutritional formula, such as we have for the production of good bones, has not been satisfactorily worked out for the production of healthy, caries-resistant teeth. Fluoridation of water and general recommendations for a complete diet are available as aids but have not kept pace with the yearly increment of dental disease.

Proper nutrition of the young should result in structurally better, sounder teeth. Once teeth are fully formed, however, their composition and properties are not appreciably affected by general bodily nutrition. In contrast to this, the periodontium, consisting mainly of gingiva and bone supporting the teeth, may reflect the present state of nutrition of the patient. In this respect, tissues of the oral cavity are similar to tissues in other parts of the body. As the

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severity of clinical and oral symptoms depends on the intensity and duration of the nutritional deficiency,[8, 8a] the modern dentist, alert to these oral changes, may detect symptoms of malnutrition in his patients at an early stage before they become irreversible. Some oral manifestations of nutritional deficiency states may express themselves as rampant decay, sore and burning mouth, cracks or fissures of the corners of the mouth, and smooth, denuded atrophic tongues with associated color changes and enlarged hyperemic gingivae.

To minimize caries development in fully formed teeth, it is necessary to make all possible reduction of the caries-inducing forces. These are thought to be acid produced by microorganisms, compounds that form un-ionized complexes with calcium (referred to as chelating agents), and possibly enzymes destroying the organic portion of the teeth.[9] The solution of the inorganic material by the formation of soluble un-ionized complexes (chelation is one method for this) can be accomplished not only in acid but in neutral and basic media as well.

While there is uncertainty as to the exact mechanism of caries production, it is generally agreed that reduction of refined sugars and starches in the diet in addition to good oral hygiene will reduce the incidence of caries.

Diet and nutrition play an important role not only in caries production and control but also in the rate of degeneration of the periodontium.[10, 11] More teeth are said to be lost from advanced periodontal disease than from caries after the age of 40.[14, 14a, 28] The causes of periodontal diseases are multifaceted, implicating both local and systemic factors. Responsible investigators agree that the most important group of systemic factors which may affect periodontal tissues are nutritional disorders.[12, 13, 14a] This may be explained in the following manner:

Materials for continuous replacement of the supporting gingiva and alveolar bone must come from the daily diet. Deficiencies of certain essential nutrients result in inadequate replacement, thus affecting the integrity of the supporting structures of the teeth. Vitamins A, B complex, C, and D, calcium, phosphorus, and protein are needed for repair of the alveolar bone, connective tissue, and epithelium which comprise the periodontium. These nutrients are woefully lacking in many of the patients' diets.[15-18]

DIETARY CONSIDERATIONS

The majority of dental patients, unless they have some organic disease which would impair the utilization and absorption of essential nutrients, can be helped by dietary guidance alone. This can be accomplished by eliminating or reducing the refined, sticky, nondetergent, "empty"-calorie[18a] foods which are implicated in the cause of caries and periodontal disease. The seven basic foods advocated by the Department of Agriculture,[19] containing all the necessary elements for repair and replacement of cellular tissue, should then be substituted for the nondetergent, "empty"-calorie foods. This procedure would

TABLE I. DIET MODIFIED FROM THE BASIC 7 FOOD GROUPS[19]

1. Leafy, green and yellow vegetables: one or more servings daily
2. Citrus fruits, tomatoes, raw cabbage, and other high vitamin C foods: one or more servings daily
3. Potatoes and other vegetables and fruit: two or more servings daily
4. Milk, cheese, ice cream
   Children and adolescents: 3 to 4 cups of milk daily
   Adults: 2 or more cups of milk daily
   Pregnant women: at least 1 quart of milk daily
   Nursing mothers: about 1½ quarts of milk daily
   Hard cheese (cheddar type): 1 oz. equals 1 cup of milk
5. Meat, poultry, fish: One serving daily:
   Eggs: one a day
   Dried beans, peas, nuts, peanut butter: two or more servings a week
6. Bread, flour, and cereals (whole-grain, enriched, or restored): Every day
7. Butter or fortified margarine: some daily

suffice for most of our patients, especially the young adults. Consumption of such a detergent, nutritious diet would also stimulate the periodontium to maintain its integrity through function (Table I).

TABLE II. HIGH-ENERGY "EMPTY"-CALORIE FOODS TO BE EATEN SPARINGLY

Bacon	Corn meal, degerminated
Drippings	Cornstarch
Lard or other shortenings	Hominy grits
Mutton fat	Macaroni
Poultry fat	Noodles
Salad dressings	Rice, white
Spaghetti	Salad oils
Salt pork, fat back	Unenriched crackers, French and
Suet	Italian white bread, and white flour
Honey	Cakes
Jams	Candies
Jellies	Chocolates
Molasses	Cocoa
Preserves	Cookies
Sirup	Pastries
Sorghum	Sugar
	Other sweets

ORAL PROCEDURES AFFECT NUTRITION

Many oral conditions and procedures, however, require supplementation with vitamins and minerals as well as special dietary guidance. These oral conditions are usually associated with emotional and physical stress which may precipitate nutritional deficiencies because of an already tenuous equilibrium that has existed for many years. Interference with the normal masticating process usually accompanies such dental procedures as soft-tissue surgery, multiple extractions, immediate dentures, new dentures, and many other dental procedures that produce stress for periods of one week to two months. Loss of blood from oral surgical procedures, as it affects the state of nutrition of a patient, has also been underestimated.

Gores, Royer, and Mann[21] collected the blood from forty-seven patients undergoing oral surgical procedures. They demonstrated that wherever extensive mucoperiosteal flaps were created with the removal of teeth and alveoloplasty, the blood loss ranged from 166 to 771 c.c. depending upon whether a

vasoconstrictor was used. Johnson,[22] at a later date, confirmed the above findings by stating that during multiple extractions and alveolotomy the volume of blood loss varied from 35 to 902 ml. It might be worth while to perform similar studies to determine the volume of blood loss during gingival surgical procedures.

Gores and associates and Johnson mention that the magnitude of the blood loss approximated that of general surgical procedures, such as gastric resection, appendectomy, herniorrhaphy, nephrectomy, simple mastectomy, cholecystectomy, hemorrhoidectomy, and pelvic surgery. One must also take into account that in some cases of oral surgery the blood loss may be as large or larger postoperatively.

Johnson[22] also reminds us that it is common knowledge that the red cell replacements, in recovery from blood loss, lag from six to eight weeks, whereas plasma volume replacements occur within twenty-four hours. He further states: "In those cases in which replacement therapy is deemed unnecessary, the postoperative therapeutic regimen should include a high quality protein diet, vitamin supplements of B complex and C and iron in the form of ferrous sulfate."

During this time of healing and/or adjustment, the inability to chew properly may so reduce the tolerance to certain types of food that important items are automatically deleted from the diet. The following is a list of dental conditions and/or procedures requiring special nutritional care:

I. Oral Surgical Procedures
   - A. Multiple extractions
   - B. Alveolectomies
   - C. Gingivectomies as well as other soft-tissue excisions, including the remodeling and removal of alveolar bone
   - D. Removal of bone cysts in the jaw or performance of other major oral surgical procedures

II. Extensive Oral Reconstructions
   - A. Preparations, with the patient under anesthesia, of multiple abutments for fixed or removable prostheses (in many cases requiring long appointments over a protracted period and thus creating a great deal of physical as well as emotional stress)
   - B. Construction of full upper or lower dentures and denture soreness which may interfere with normal masticatory function and selection of nutritious diets

III. Conditions Other Than Elective Surgical or Reconstruction Procedures
   - A. Oral symptoms of unknown etiology, such as burning mouth and tongue or generalized pain in and around the oral cavity
   - B. Obvious signs of nutritional deficiencies, such as cheilosis, perlèche, angular stomatitis, and red, beefy, magenta, or slick tongue[20]

C. Patients for whom antibiotics which may precipitate nutritional deficiencies were prescribed

D. Oral conditions of unknown etiology in which multivitamin supplementation may be prescribed as adjunctive therapy, such as: recurrent necrotizing ulcerative gingivitis, desquamative gingivosis, leukoplakia, lichen planus, recurrent aphthae, and herpetic ulcerative gingivostomatitis

The foregoing oral conditions and dental procedures warrant supplementation with crystalline multivitamins as well as dietary guidance because they are associated with stress, because the patients are usually emotionally disturbed by such stressful procedures, because there may be a loss of blood volume of from 35 to 900 ml.[21, 22] (especially during surgical procedures as well as a possible similar volume of blood loss postoperatively), and because there may be an interference with normal masticatory function which may alter the patient's selection and ingestion of nutritious foods.

According to Ravdin and Zintel,[23] the importance of adequate nutrition in the patient requiring extensive surgical or operative procedures cannot be overemphasized. These authors also believe that when the dietary intake of a previously healthy person is markedly reduced for as little as ten to twelve days, there may occur vitamin deficiencies which can reduce physical fitness, reduce resistance to disease, and interfere with normal wound healing. Even though clinically recognizable vitamin deficiencies are rare, there is not sufficient appreciation of the fact that a subclinical vitamin deficiency may cause profound disturbances of the physiologic processes of the body.

TABLE III. SAMPLE HIGH-PROTEIN LIQUID DIET

Breakfast:	Orange juice, oatmeal with hot milk, butter, and sugar, coffee with cream and sugar
Mid-morning:	Eggnog or proprietary protein supplement*
Noon meal:	Cream of asparagus soup, tomato juice with tablespoon of Brewer's yeast, baked custard, milk, tea with sugar, juice of one lemon
Mid-afternoon:	Ginger ale and grapejuice with egg white or proprietary protein supplement
Evening meals:	Beef broth with egg;† grapefruit juice, junket, hot chocolate with milk
Bedtime:	Eggnog with vanilla ice cream or proprietary protein supplement (meritene or sustagen)

*Protein supplement following surgery:

4 eggs
½ tablespoon sugar
1 quart milk
1 cup skim milk powder

Beat eggs with sugar, add milk, and mix. Sprinkle milk powder over milk-egg mixture and beat until smooth. Flavor with vanilla. Chill thoroughly before serving. Keep refrigerated.

Proprietary prepared protein supplements (meritene or sustagen) may be substituted for the eggnog.

†To prepare broth with egg, add ⅔ cup hot broth gradually to one slightly beaten egg, stirring continuously; serve at once.

THERAPEUTIC PROCEDURES

Dietary guidance and supplementation may be of considerable help during periods of stressful dental procedures. Because of their soft consistency and ease in swallowing, the following foods may be permitted during periods of stress

due to elective soft-tissue surgery, multiple extraction, major oral surgical procedures, or periods of adjustment to new prostheses: broth, tea, eggnog, ginger ale, cooked cereals, coffee, cocoa, sugar, custard, junket, clear gelatin, strained soups, plain ice cream, cottage cheese, farmer or pot cheese (unlimited), strained meats, vegetables, and juices (may be obtained from prepared baby foods and seasoned to taste), and supplemental feedings of proprietary protein or milk preparations. Along with dietary guidance, crystalline vitamin supplements may be prescribed.

Pollack and Halpern[27] caution: "Vitamins are adjuvants and their usage should never divert attention from the total nutrition of the patient. Vitamin deficiency, however, should never be allowed to become a contributing factor in prolonging convalescence." They recommend stress vitamins for maximum effective therapy as follows:

Stress Vitamin Capsule

Thiamine hydrochloride	10 mg.	Pyridoxine hydrochloride	2 mg.
Riboflavin	10 mg.	Folic acid	1.5 mg.
Niacinamide	100 mg.	Ascorbic acid	300 mg.
Calcium pantothenate	20 mg.	Vitamin B_{12}	4 mcg.
Vitamin K	2 mg.		

The dentist should assume that all patients are nutritionally deficient to some extent, since the vitamin status of the patient's tissues cannot be determined clinically. When elective oral surgical or extensive reconstructive procedures are anticipated, it would be advisable to prescribe two of the stress vitamin capsules or tablets along with two tablets of 250 mg. of vitamin C daily, to be taken with meals one week before and for one week after the operative procedures are completed. After the first week postoperatively, one capsule of the stress vitamins and one 250 mg. tablet of vitamin C daily should be sufficient until masticatory function is regained and oral tissues return to normal.

As stated previously, the majority of our patients require guidance in supplying essential dietary allowances of all the recommended nutrients. If there is any doubt, however, about the adequacy of the current diet or of the previous diet, one or two tablets per day of a maintenance vitamin tablet may be prescribed as follows:

Maintenance Vitamin Tablet

Thiamine hydrochloride	3 mg.	Pyridoxine hydrochloride	0.5 mg.
Riboflavin	3 mg.	Folic acid	0.5 mg.
Niacinamide	30 mg.	Vitamin B_{12}	4.0 mcg.
Ascorbic acid	100 mg.	Vitamin A	5,000 units
Calcium pantothenate	5 mg.	Vitamin D	400 units
Vitamin K	2 mg.		

The maintenance vitamin tablet should be prescribed for those patients suspected of having poor nutrition; they should be taken until the dentist notices that the oral tissues respond within normal limits.

SUMMARY AND CONCLUSION

1. Caries and periodontal disease are widespread. In 1956 80,000 dentists could give adequate but not optimum care for only 35 per cent of 170,000,000 persons. Improved nutrition through proper diet is the safest and best method to reduce the initiation and progression of dental disease for the population of 228,000,000 expected by 1975.

2. To minimize development of caries and periodontal disease for all age groups, patients should be advised by their dentists to eliminate from their daily diet all the refined, sticky, nondetergent, empty-calorie foods. By simply substituting the seven basic foods advocated by the Department of Agriculture, all the necessary elements for repair and replacement of cellular tissue will be present and the diet will be detergent.

3. Oral procedures associated with emotional and physical stress may precipitate nutritional deficiencies because of a pre-existing tenuous equilibrium. Soft-tissue surgery, multiple extractions, immediate dentures, new dentures, and many other dental procedures may produce stress for periods of one week to two months. These patients require high-protein diets as well as vitamin supplements.

4. Loss of blood from oral surgical procedures, as it affects the state of nutrition of the patient, has been underestimated. Recent investigations have demonstrated that such blood loss ranged from 35 to 902 ml. The volume of blood loss approximated that of such general surgical procedures as gastric resection, appendectomy, herniorrhaphy, and nephrectomy. In some cases the postoperative blood loss was said to be as large or larger.

5. Plasma volume replacements occur within twenty-four hours. However, there is a lag of from six to eight weeks for red cell replacements. There are also losses of other important cellular nutrients. Therefore, it would be prudent for the oral surgeon as well as those performing gingival and soft-tissue surgery and remodeling of alveolar bone to prescribe a high-protein diet and vitamin supplements preoperatively and postoperatively.

6. It is assumed that the dentist will have consulted the patient's physician to be sure that there are no contraindications for the prescription of diets or vitamin supplements. It is also understood that vitamin supplements will not cure dental diseases or overcome ineffective diagnoses and dental procedures. Minerals and trace elements have not been considered in the present article, since the requirements are very small and are usually supplied even in the most restricted diets of patients undergoing dental operations.

7. The dentist is in an enviable position to detect early oral signs of nutritional deficiencies. This can be of inestimable value to both the physician and the patient. Until such time as dental disease can be prevented, the combined efforts of the health services, the government, and the public must be enlisted to repair oral disease and preserve oral health in order to add years to our patients' lives and life to the years of our aging population.

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PHARMACOLOGY AND THERAPEUTICS

CLINICAL EVALUATION OF LEVO-NORDEFRIN IN LOCAL ANESTHETICS

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NORDEFRIN has been employed for many years as a vasoconstrictor in anesthetic solutions and has found wide acceptance among members of the dental profession. This compound, like epinephrine, levarterenol, phenylephrine, and many other sympathetic amines, exists in optical isomeric forms and hence can be resolved into dextrorotatory and levorotatory isomers. In each case it has been found that substantially all of the cardiovascular activity resides in the levo form. Although the dextro isomer may have some pharmacodynamic effects of its own, such activity is always at a very low level and furthermore may differ qualitatively as well as quantitatively from the much more active levo compound.

Until recently, nordefrin has been available commercially only in the racemic form, which of course contains exactly equal quantities of the optical isomers. In 1957 anesthetic solutions containing the pure levorotatory compound were introduced as levo-nordefrin. The pharmacologic properties of this compound, as well as the corresponding dextro isomer, have been reported by Luduena and co-workers.[1] A preliminary report on the use of levo-nordefrin as a vasoconstrictor in local anesthetic solutions has been made by Dobbs.[2, 3] In order to evaluate further the clinical usefulness of levo-nordefrin, I set up a study in the student clinics of this dental school. The results obtained will be presented in this article.

In common with other studies on local anesthetic solutions in this college, we have employed the so-called "blind test" procedure. This approach to the clinical evaluation of anesthetic solutions is considered vital in order to eliminate the rather substantial subjective factor that greatly influences judgment. The details of this method have been published previously[4] and are sufficiently well known and understood that they need not be repeated here.

The patients were selected at random in both the operative and the surgical clinics. All injections were administered by junior and senior students. Three

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All solutions used in this study were supplied by Cook-Waite Laboratories, Inc., as follows: nordefrin (Cobefrin), levarterenol (Levophed), phenylephrine (Neo-Synephrine), levo-nordefrin (Neo-Cobefrin), propoxycaine (Ravocaine), and procaine (Novocain).

different anesthetic solutions were used in more than 1,600 patients. The accuracy with which the solution was deposited at the proper site may not be as great as if the injections had been made by seasoned practitioners. Because of this, comparisons should not be made between the absolute values reported here and similar data obtained in other studies by more experienced clinicians. This would not impair the validity of any comparisons which might be drawn between the three solutions within this study, however, since all three solutions were administered by all of the operators.

The observations made by each operator were recorded on special printed cards designed specifically for this study. This helped to ensure that the specific observations which were of interest in this study would not be forgotten or overlooked by the operator. This procedure also helped to minimize the occurrence of incomplete records. The cards were turned in to an instructor at the end of each day and checked for completeness. They were then turned over to a trained statistician who decoded the solutions, assembled the data, and made the necessary standard statistical calculations. It was not until the project had been completed that anyone connected with the study saw the key to the code employed.

The active components of the three solutions employed in this study were as follows:

(A) *RNC*	
propoxycaine hydrochloride	0.4 per cent
procaine hydrochloride	2.0 per cent
nordefrin (racemic)	1:10,000
(B) *RNN*	
propoxycaine hydrochloride	0.4 per cent
procaine hydrochloride	2.0 per cent
levo-nordefrin	1:20,000
(C) *NE*	
procaine hydrochloride	2.0 per cent
epinephrine	1:50,000

When one considers solutions A and B, it is seen that the only variable in the vasoconstrictor, so that in this pair we were comparing nordefrin, which is the racemic compound, with levo-nordefrin, which is the pure levo isomer. Concentrations of 1:10,000 and 1:20,000, respectively, were used since, on the basis of theoretical considerations, these two concentrations should be equivalent. Furthermore, the pharmacologic data which have been reported[1] tend to confirm this. The procaine-epinephrine solution (C) was included in the study solely as a standard for comparison, since it has been used for this purpose in many other studies reported in the literature and from this college.

The data obtained have been assembled in two ways. First, all the cases have been combined, irrespective of whether procedures performed were surgical or operative and without regard to the type of injection employed. In Table IV the cases have been segregated into either surgical or operative. The

reason for this lies in the fact that many clinicians feel that it is more difficult to obtain completely satisfactory anesthesia for cavity preparations than it is for exodontia or other surgical procedures.

In Table I are recorded the values for volume of solution used, onset time of anesthesia, and duration of anesthesia for all of the cases. The results are expressed as averages plus or minus the standard error of the average. It can be seen that the distribution of cases between the three solutions is very nearly equal. The number of patients varies slightly across the table due to the fact that the record cards were occasionally incomplete for one observation or another. For example, in the case of solution RNC the volume of solution employed was recorded for all 544 cases. The onset time was recorded for only 534 cases, however, which means that this observation was not recorded on ten of the case record cards.

TABLE I. AVERAGE VOLUME OF SOLUTION USED, ONSET TIME, AND DURATION OF THE THREE ANESTHETIC SOLUTIONS — COMBINED RESULTS

	VOLUME (C.C.)		ONSET TIME (MINUTES)		DURATION (MINUTES)	
SOLUTION	NO. OF PATIENTS	AVERAGE ± STANDARD ERROR	NO. OF PATIENTS	AVERAGE ± STANDARD ERROR	NO. OF PATIENTS	AVERAGE ± STANDARD ERROR
RNC	544	2.71 ± 0.07	534	2.77 ± 0.12	539	121.95 ± 2.85
RNN 1:20,000	470	2.88 ± 0.08	466	2.87 ± 0.14	433	154.69 ± 3.69
NE	540	2.52 ± 0.05	524	2.91 ± 0.12	536	114.17 ± 2.74

Differences in the volume of solution used for the three formulations are minor and probably are not significant. The same may be said for the onset time of anesthesia. With regard to duration of anesthesia, the differences again are not large but are probably statistically significant. It should also be kept in mind that probably there is a greater error involved in measuring this parameter than any of the others.

Table II summarizes the combined results for grade of anesthesia and amount of bleeding. For purposes of this study, Grade A implies that the degree of anesthesia was completely satisfactory. Grade B represents those cases in which anesthesia was not complete; some pain was present but not enough to require reinjection. Those cases in which pain was sufficient to require a second injection were recorded as Grade C. It is apparent that RNN solution gave the highest incidence of Grade A, or completely satisfactory, anesthesia. RNC was second in this respect, but the differences between the two are probably not significant. Both solutions were very definitely superior to the procaine-epinephrine solution, however, and the differences here are large enough to be statistically significant. With regard to the amount of bleeding which occurred, procaine-epinephrine gave the highest incidence of no bleeding and the lowest incidence of excessive bleeding. RNC and RNN were about the same.

TABLE II. GRADE OF ANESTHESIA AND INCIDENCE OF BLEEDING—COMBINED RESULTS

	GRADE OF ANESTHESIA					BLEEDING					
SOLUTION	NO. OF PATIENTS	PER CENT A ± S.E.	PER CENT B ± S.E.	PER CENT C ± S.E.	NO INFORMATION (PER CENT)	NO. OF PATIENTS	NONE ± S.E.	PER CENT SLIGHT ± S.E.	PER CENT MODERATE ± S.E.	PER CENT EXCESSIVE ± S.E.	NO INFORMATION (PER CENT)
RNC	572	79.7 ± 1.72	8.4 ± 1.16	10.7 ± 1.29	1.2	576	50.7 ± 2.08	21.4 ± 1.71	17.0 ± 1.59	5.7 ± 0.97	5.2
RNN 1:20,000	501	81.6 ± 1.73	5.0 ± 0.97	13.0 ± 1.50	0.4	503	45.9 ± 2.22	27.2 ± 1.98	17.5 ± 1.69	4.6 ± 0.93	4.8
NE	553	66.7 ± 2.00	13.9 ± 1.47	17.9 ± 1.63	1.4	558	69.7 ± 1.95	17.9 ± 1.62	7.2 ± 1.09	2.0 ± 0.59	3.2

TABLE III. INCIDENCE OF SYSTEMIC AND LOCAL REACTIONS—COMBINED RESULTS

SOLUTION	NO. OF PATIENTS	SYSTEMIC REACTIONS*													LOCAL REACTIONS*						
		PER CENT NONE ± S.E.	PER CENT TREMOR ± S.E.	PER CENT PALPITATION ± S.E.	PER CENT PERSPIRATION ± S.E.	PER CENT NAUSEA ± S.E.	PER CENT FAINTING ± S.E.	PER CENT HEADACHE ± S.E.	PER CENT NERVOUSNESS ± S.E.	PER CENT TEARS ± S.E.	PER CENT DIZZINESS ± S.E.	PER CENT WEAKNESS ± S.E.	PER CENT OTHER ± S.E.	NO INFORMATION (PER CENT)	PER CENT NONE ± S.E.	PER CENT IRRITATION ± S.E.	PER CENT EDEMA ± S.E.	PER CENT SWELLING AT INJECTION SITE ± S.E.	PER CENT EXCESSIVE PAIN, SORENESS ± S.E.	PER CENT OTHER ± S.E.	NO INFORMATION (PER CENT)
RNC	575	91.5 ±	1.7 ±	0.7 ±	0.9 ±	1.6 ±	2.3 ±	0	0.3 ±	0	0	0	0.2 ±	1.9	84.2 ±	1.4 ±	0.7 ±	0.2 ±	1.0 ±	0.5 ±	13.6
	S.E.	1.16	0.54	0.35	0.39	0.52	0.63		0.23				0.19		1.52	0.49	0.35	0.19	0.41	0.29	
RNN 1:20,000	503	92.8 ±	1.0 ±	1.2 ±	0.8 ±	1.2 ±	1.4 ±	0.2 ±	0	0	0.2 ±	0.4 ±	0.4 ±	2.4	88.3 ±	1.0 ±	0.2 ±	0.8 ±	1.6 ±	0.2 ±	9.1
	S.E.	1.15	0.44	0.49	0.40	0.49	0.52	0.20			0.20	0.28	0.28		1.43	0.44	0.20	0.40	0.56	0.20	
NE	558	92.1 ±	2.3 ±	2.0 ±	1.4 ±	1.3 ±	0.7 ±	0.2 ±	0	0.2 ±	0.2 ±	0	0.4 ±	1.3	87.5 ±	1.3 ±	0.4 ±	0.9 ±	1.3 ±	0.7 ±	9.7
	S.E.	1.14	0.63	0.59	0.50	0.48	0.35	0.19		0.19	0.19		0.27		1.40	0.48	0.27	0.40	0.48	0.35	

*The total per cent is greater than 100 since some patients had more than one reaction.

Table III records the incidence of various systemic reactions observed during the time that the patient was in the chair. RNN solution containing the levo isomer of nordefrin showed the highest incidence of "no reactions" and the lowest incidence of perspiration, tremor, and nausea. One incidence of headache occurred with procaine-epinephrine and also with RNN. It is interesting to note that with both RNN and RNC it is possible to achieve a significantly higher incidence of Grade A or completely satisfactory anesthesia without sacrificing safety as measured by the criterion of systemic reactions. The same conclusion may be drawn when one uses the criterion of local reactions also recorded in Table III. Here again, RNN produced the highest incidence of freedom from local intolerance of the three solutions tested.

In Table IV the cases are divided according to operative or surgical procedures. The volume of solution employed for surgical cases was uniformly higher than for the operative ones. Both RNC and procaine-epinephrine gave a shorter duration for surgical cases than for operative cases. RNN, on the other hand, gave a longer duration for the surgical group. The reasons for these differences are not obvious.

TABLE IV. CLINICAL RESPONSES ACCORDING TO TYPE OF PROCEDURE IN 1,017 OPERATIVE PATIENTS AND 619 SURGICAL PATIENTS

PROCEDURE AND SOLUTION	VOLUME (C.C.) AVERAGE ± S.E.	ONSET TIME (MINUTES) AVERAGE ± S.E.	DURATION (MINUTES) AVERAGE ± S.E.	DEGREE OF GRADE A ANESTHESIA PER CENT ± S.E.	NO REACTIONS PER CENT ± S.E.	
					SYSTEMIC	LOCAL
Operative						
RNC	2.24 ± 0.05	2.73 ± 0.17	141.53 ± 3.54	76.76 ± 2.34	94.83 ± 1.22	96.66 ± 0.99
RNN 1:20,000	2.22 ± 0.05	2.89 ± 0.22	141.98 ± 4.53	77.33 ± 2.79	95.58 ± 1.37	91.59 ± 1.85
NE	2.34 ± 0.04	2.90 ± 0.13	121.04 ± 3.06	63.02 ± 2.56	93.94 ± 1.11	93.94 ± 1.11
Surgical						
RNC	3.35 ± 0.12	2.83 ± 0.16	94.41 ± 4.05	83.67 ± 2.36	86.99 ± 2.14	67.48 ± 2.99
RNN 1:20,000	3.45 ± 0.13	2.86 ± 0.17	165.50 ± 5.54	85.14 ± 2.14	90.61 ± 1.75	85.56 ± 2.11
NE	3.41 ± 0.20	2.98 ± 0.28	81.01 ± 4.68	84.38 ± 3.71	83.33 ± 3.80	56.25 ± 5.06

The incidence of completely satisfactory anesthesia is greater in the surgical group than in the operative group, confirming the general impression in this regard. The differences in Grade A anesthesia for the two groups of patients is less marked between RNC and RNN than it is between these two solutions and procaine-epinephrine. This probably reflects the considerably higher potency of the propoxycaine-containing solutions. It is further worthy of comment that when an extra demand for deep anesthesia is placed on a solution, as in the operative cases, the less potent procaine-epinephrine cannot measure up to the requirements. In these cases a more satisfactory incidence of Grade A anesthesia can be met only by the use of more potent agents. The superiority

of both RNN and RNC over procaine-epinephrine for operative cases is well beyond the range of experimental error and therefore must be considered as real. The incidence of systemic reactions in the operative group is lowest with RNN, followed by RNC and NE in that order. This same order is followed in the surgical group. Since systemic reactions may be taken as a measure of clinical toxicity, it seems clear that during the past few years dental research has kept pace with technologic advances in other fields and has presented the clinician with vasoconstrictors and local anesthetic agents which are capable of providing increased comfort for the patient without a decrease in safety.

Generally speaking, the incidence of systemic reactions is higher for the surgical patients than for the operative ones. Many of the systemic reactions listed, such as tremor, palpitation, perspiration, nausea, fainting, and nervousness, are undoubtedly largely psychic in origin. The higher incidence of such reactions in the surgical group is therefore to be anticipated, since such patients are much more likely to be apprehensive and agitated than those who present themselves for operative procedures. A higher incidence of local reactions is also to be expected in the surgical group, since the degree of trauma and insult to the tissues is much greater than with operative procedures. It is interesting to note that in this surgical group, where a higher incidence of both systemic and local reactions is to be expected, RNN uniformly gives the highest percentage of "no reactions." In the case of local reactions, this difference is statistically significant, although the differences may not be real in the case of systemic reactions.

SUMMARY AND CONCLUSIONS

A clinical study has been made of a new local anesthetic solution containing levo-nordefrin. It was compared with the racemic form of the same vasoconstrictor and also with epinephrine, the latter in a different anesthetic solution. Injections of each solution were made in more than 500 patients by students in the dental clinic. The following conclusions were drawn from the data obtained:

1. In comparison with nordefrin in a solution otherwise identical in composition, levo-nordefrin produces a slightly higher incidence of Grade A anesthesia, although this difference is probably not significant.

2. Of the three solutions tested, the formula containing levo-nordefrin produced the lowest incidence of both systemic and local reactions, but here again the difference may not be significant.

3. In general, the solutions containing both nordefrin and levo-nordefrin permit a somewhat higher incidence of bleeding when compared to a procaine solution containing epinephrine 1:50,000. This would seem to suggest that both nordefrin at 1:10,000 or levo-nordefrin at 1:20,000 are milder vasoconstrictors at these levels than epinephrine at a concentration of 1:50,000.

4. Specific information on a number of systemic and local reactions was tabulated for each solution. Differences between the three solutions were minor and not statistically significant. All three solutions were considered to be well tolerated.

5. Another vasoconstrictor—levo-nordefrin—has been clinically evaluated in this study in comparison with nordefrin and epinephrine. It has been found to be an effective and safe agent for use in local anesthetic solutions when combined in a formula containing procaine and propoxycaine as the local anesthetics.

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ORAL ROENTGENOLOGY

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ELECTROLYTIC PRECIPITATION OF ZINC CARBONATE IN THE JAW

An Unusual Complication After Root Resection

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ROOT resection together with the insertion of an apical seal of silver or copper amalgam filling, is nowadays, along with conservative therapy, a routine method of treatment of periapical osteitis. The result of experimental and clinical work indicates that the tissues tolerate at least the silver amalgam to a reasonable extent.

This article represents a study, utilizing biophysical techniques, of unusual complications after root resections.

CASE REPORT

The patient was E. H., a 44-year-old woman.

In 1952 a fixed bridge was constructed in the upper jaw, extending from the right first molar to the left first molar, with ponties replacing the right canine and the left premolars. Before the bridge was made, the right lateral incisor had a post which was fixed in the root canal by a pin. A roentgenogram (Fig. 1) taken in 1951 shows that there is no root-filling material visible apical to the post and there are no positive roentgenologic signs of periapical osteitis.

The bridge was inserted on Oct. 30, 1952. Some months later, on Feb. 6, 1953, the patient came to the Royal Dental School in Malmö complaining of pain in the front of the maxilla. In the buccal region of the right lateral incisor there was a slight redness of the mucous membrane; a marked tenderness was noted on palpation. There was no swelling or fistula. Roentgen examination revealed destruction of the lamina dura in the periapical region of the right lateral incisor. This destruction was most evident mesial to the apex (Fig. 2).

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This investigation has been supported by a financial grant D-700 from the National Institute of Health, Bethesda, Maryland, U.S.A., to the Department of Medical Physics, Karolinska Institutet, Stockholm, Sweden.

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One week later, on Feb. 12, 1953, the periapical bone destruction had increased but was not so well defined (Fig. 3). Within a small area at the apex, however, the bone showed normal structure, which indicated the formation of a sequestrum.

Because of the roentgenologic findings, a root resection was performed on the right lateral incisor. The apical opening of the root canal was obliterated by a silver amalgam filling. The incision healed by primary union.

Fig. 4 shows a roentgenogram taken after the operation on Feb. 21, 1953. Three months later (May 20, 1953), the apex was surrounded by a well-defined roentgenolucent area (Fig. 5). Above, beside, and below the amalgam filling there was a roentgenopaque area which was demarcated against its surroundings. Distal to the root there were two small roentgenopaque fragments (possibly amalgam) near the alveolar crest.

About one year later (June 15, 1954) the destruction had extended further, particularly distally. Its roentgenolucency was more pronounced, indicating that the pathologic area had become limited (Fig. 6). The roentgenopaque area around the apex had also increased and showed greater contrast to the normal bone. The roentgenopaque substance was not homogenic but seemed to be deposited in irregular layers around the apex and the amalgam filling.

Another surgical procedure was undertaken, and the root was resected to the post. The diseased tissues were removed, and a new silver amalgam filling was inserted. The wound was sutured. The extent of the operation is evident from the roentgenogram shown in Fig. 7.

The postoperative course was clinically without complications. Three months later, however, on Sept. 21, 1954, a new roentgenogram (Fig. 8) revealed that bone destruction was still continuing. Close to the amalgam filling there was a small roentgenopaque and homogenic area. Around this area but at some distance from it there was, in addition, some roentgenopaque substance.

A few months later, on Jan. 25, 1955, the destruction had extended toward the alveolar crest and had reached further toward the nasal cavity. The amount of roentgenopaque substance around the apex had also increased (Fig. 9).

In a third operation (Jan. 26, 1955) the whole root and the surrounding supporting tissues were removed. Clinically, no signs of malignancy could be detected. The postoperative roentgenogram is shown in Fig. 10.

It appeared that the roentgenopaque substance was connected with the complications experienced in this case, and therefore a part of this material was subjected to analysis.

Investigations of the Removed Pathologic Tissues.—The specimens from the operations of June 15, 1954, and Jan. 26, 1955, were fixed in 10 per cent formalin, decalcified in formic acid, and passed through the routine histologic process.

The roentgenopaque specimen, which was 1 mm. in diameter, was embedded in methylmethacrylate. After polymerization, thin sections were prepared for subsequent analysis by microroentgenography and roentgen diffraction. (For reference to the technical procedures, see Engström, Björnerstedt, Clemedson, and Nelson.[4])

Histopathologically, there was in both cases a nonspecific inflammation with an invasion of plasma cells and giant cells. Scattered through the tissue were areas of hyaline degeneration (Fig. 11). Around the necrotic areas there was no evidence of foreign body reaction. These pathologic changes were more advanced in the specimen removed at the last operation (Jan. 26, 1955).

In addition to the classical signs of a chronic inflammation, there were, in the specimen removed at the operation of June 15, 1954, numerous small rodlike crystals scattered through the tissue (Fig. 12). These crystals gave a negative response to a histochemical test for iron.

The microroentgenogram of the roentgenopaque substance showed a somewhat "blistered" structure (Fig. 13). Light and dark areas indicate varied absorption of the

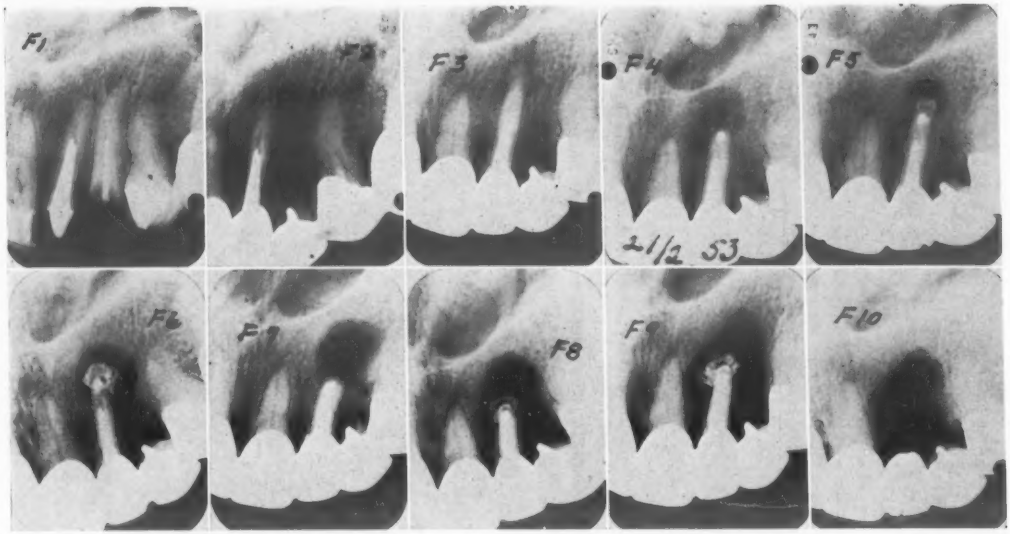

Fig. 1.—No root-filling material visible in the lateral incisor, with the exception of the metal post. There are no signs of osteitis around the apex. Feb. 17, 1951.

Fig. 2.—Destruction of the lamina dura at the apex of the lateral incisor. The destruction is most marked mesial to the root. Feb. 6, 1953.

Fig. 3.—Bone destruction around the apex of the lateral incisor and possibly a sequestrum formation at the apex. Feb. 12, 1953.

Fig. 4.—Roentgenogram taken after the operation. Feb. 21, 1953.

Fig. 5.—The apex of the right lateral incisor surrounded by a well-defined bone destruction. There is a roentgenopaque area close to the amalgam filling. May 20, 1953.

Fig. 6.—The bone destruction at the right lateral incisor as well as the roentgenopaque area has increased in size. June 15, 1954.

Fig. 7.—Roentgenogram taken after the second root resection of the right lateral incisor. June 15, 1954.

Fig. 8.—New deposition of roentgenopaque substance at the apex of the right lateral incisor. Sept. 21, 1954.

Fig. 9.—There is still an increase in both the bone destruction and the roentgenopaque formation at the apex of the right lateral incisor. Jan. 25, 1955.

Fig. 10.—Roentgenogram taken after the last operation. Jan. 26, 1955.

roentgen radiation. The absorption seemed to be greatest in the periphery of the specimen. Separate layers or concentrically arranged laminae could not be detected. There were no cell spaces or signs of vascularization.

Fig. 11.

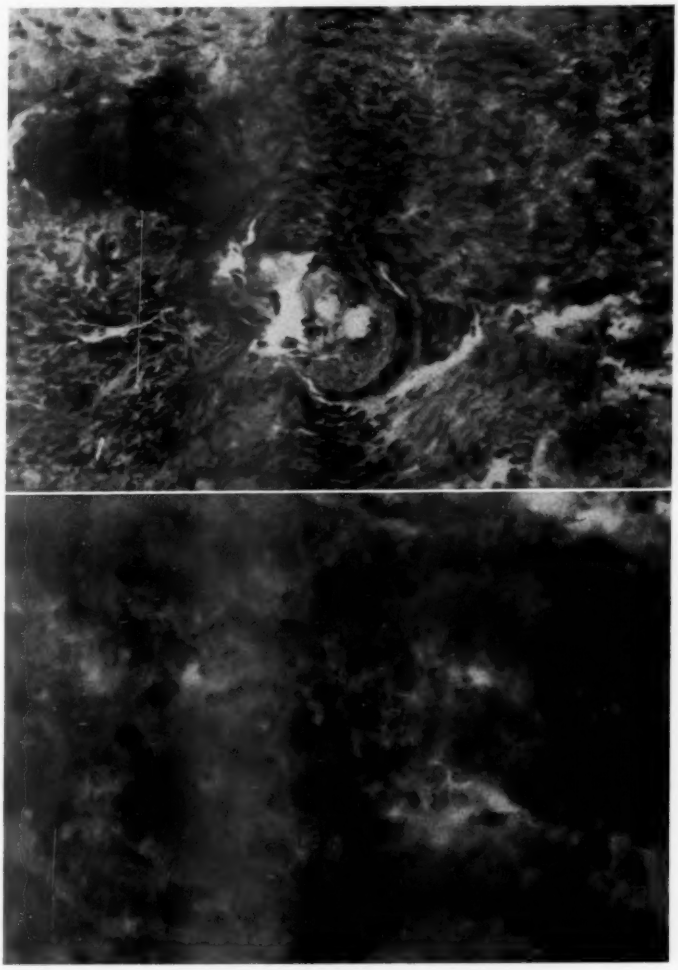

Fig. 12.

Fig. 11.—Areas with hyaline degeneration in different stages of necrosis. (Hematoxylin and eosin stain. Magnification, ×100; reduced ¼.)

Fig. 12.—Rodlike crystals scattered through the soft-tissue specimen (from the operation of June 15, 1954). (Hematoxylin and eosin stain. Magnification ×400; reduced ¼.)

The roentgen diffraction examination of the roentgenopaque substance (Fig. 14) indicated small crystals (about 10^{-5} cm.) without preferential orientation. The diffraction pattern had no resemblance to those normally found in calcified tissues (hydroxy apatite).

Fig. 13.—Microroentgenogram of a thick section of the roentgenopaque substance 100 μ thick at the apex of the right lateral incisor. Varied roentgen absorption within the specimen but no signs of separate layers. (20 kv., Eastman Spectroscopic Plate No. 649.) (Magnification, ×115; reduced ¼.)

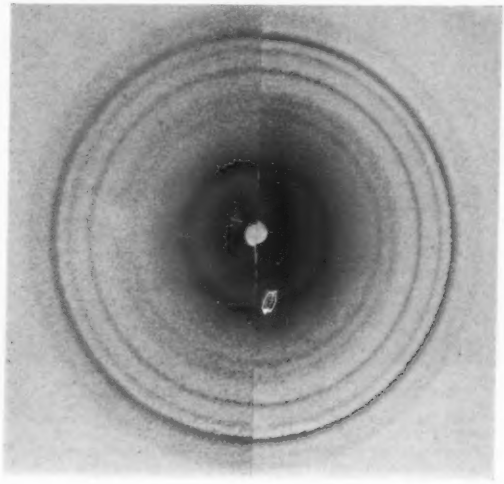

Fig. 14.—Flat-film roentgen diffraction pattern of roentgenopaque substance at the apex of the lateral incisor (left) and from a basic zinc carbonate (right). Note that the diffraction lines correspond in detail. (Ni-filtered Cu-radiation.)

When the roentgen diffraction was recorded on the heated specimen, the well-defined lines in the diffraction pattern could be assigned without doubt to a zinc oxide. With this information, the diffraction lines in the nonheated specimen could be shown to be derived from zinc carbonate.

DISCUSSION

The roentgenograms first indicated that the roentgenopaque area around the apex of the upper right lateral incisor would consist of mineral salts usually found in the mammalian organism. Such mineral deposits are generally associated with the presence of tumors, cysts with concrements,[2] or dental calculus.

Clinically, however, no signs of such pathologic changes were detected. Because of the doubtful situation, the pathologic area which had to be removed for clinical reasons was subjected to a thorough analysis. This resulted in the surprising disclosure that the roentgenopaque deposition consisted mainly of zinc carbonate.

The zinc carbonate most probably was deposited by an electrolytic process, and such processes are known to develop in bone when metals forming electric elements are present.[1, 3]

Physiologically, zinc occurs in trace amounts in the organism, but it does not seem possible to reach such concentrations as were detected in this case. In all probability, the zinc ions were derived from the silver amalgam filling (containing about 1 per cent zinc), where zinc is the element which has the lowest solution potential. However, there also exists a possibility that the zinc ions in this roentgenopaque substance came from the root canal post.

Among many hundreds of cases treated in the same manner and followed up with postoperative roentgen examinations, only this one has reacted in the way described.

SUMMARY

An unusual complication after root resection of an upper lateral incisor in a middle-aged woman is described. There was bone destruction together with deposition of a roentgenopaque substance around the silver amalgam filling which had been inserted in the apical opening of the root canal after resection, and this substance reappeared after a second root resection. The increase of deposited material was studied by a series of roentgen examinations.

Microroentgenography and roentgen diffraction investigations revealed that the roentgenopaque substance consisted of zinc carbonate. It is suggested that the zinc salt was deposited as a result of an electrolytic process.

The author is much indebted to Dr. G. Björkman, Malmö General Hospital, Malmö, to Dr. D. Carlström, the Department of Medical Physics, Karolinska Institutet, Stockholm, for discussion, and to Miss K. Bergendahl for technical assistance. Thanks are due to Dr. G. Gustafson, Head of the Department of Dental Histopathology, who permitted the specimen to be sectioned in his department.

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RELATIONSHIPS OF THIRD MOLAR ROOTS TO THE MANDIBULAR CANAL

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EVERY dentist realizes the importance of avoiding injury to the inferior alveolar nerve during surgery. Such injuries frequently result in paresthesia or anesthesia of the lip accompanied by disagreeable symptoms. Most of these cases result from surgical procedures involving the mandibular third molars; the proximity of the root ends to the inferior alveolar nerve is responsible for this. Severance of nerve fibers may result in a permanent anesthesia of the lower lip if deposition of bone occurs between the ends of the severed nerve; under such circumstances, it is often impossible for the severed nerve endings to become anatomically united again. The patient's reaction to anesthesia caused by surgery is usually unfavorable, especially if the patient is not forewarned. Therefore, it becomes important for every dentist to be familiar with roentgenographic findings which suggest the possibility of disturbing the inferior alveolar nerve during surgical procedures. If the probability of nerve trauma is known, the patient can be advised preoperatively; if paresthesia or anesthesia does result, the attitude of the patient is not likely to be hostile.

Fortunately, there are several diagnostic criteria which enable one to determine the relationship of third molar roost to the mandibular canal; those which are apparent in the roentgenogram will be discussed. The intraoral dental film is most suitable for examining the third molar region. It gives the best definition of the mandibular canal, the clearest view of the outline of the molar roots, and the best opportunity to study the continuity of the root canals as they extend from the pulp chamber in the crown of the tooth to the apices of the roots. Other projections, including extraoral films, furnish valuable information, but they do not allow as detailed a study of the area as do the periapical films.

The normal unobstructed course of the mandibular canal is downward and forward from the mandibular foramen to the mental foramen. The canal is usually toward the buccal side of the mandible in the third molar area. The reason for this position can be understood if one recognizes that the

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buccal divergence or flare of the ascending ramus of the mandible places the mandibular foramen lateral to the buccal plane of the mandibular molars. When the mandibular third molar crown is inclined lingually, the root ends extend buccally. This results in an unusually close relationship between the tooth apices and the mandibular canal. Surgical intervention most frequently injures the contents of the mandibular canal when the molar tooth is tipped lingually; this is true whether the tooth is in a semihorizontal or vertical position.

Mesial and distal curvatures of the roots do not often result in disturbances to the nerve, but lateral curvatures of the roots may cause them to project against or under the mandibular canal. Whenever the shadows of the roots appear to cross the canal, partial or complete encirclement must be considered, and a surgical technique which allows the operator to care adequately for such possibilities (Fig. 1) must be employed. A lateral curve in the root is indicated in the roentgenogram by a rounded and almost blunt

Fig. 1.—The apices of the third molar partially encircle the mandibular canal.

appearance of the root end; this represents the curved apical section of the root. The apical foramen and the portion of the canal running buccally or lingually appears as a small, central, circular black dot surrounded by a circumscribed roentgenopaque area. Incidentally, the diameter of this area indicates the width of the root. When such curvature occurs above the mandibular canal, it is only a surgical problem. When it occurs below the canal, however, the contents of the mandibular canal may be disturbed by tooth removal.

The possibility of the nerve passing between the roots must be considered when two or more roots extend below the canal (Fig. 2). Divergence of the root canals from the pulp chamber around the mandibular canal, followed by partial or complete fusion of the canal apically, may indicate this possibility (Fig. 3). The root ends may be closely contacting, or they may be actually fused together. The characteristic appearance of the nerve passing through the roots shows the shadow of the roots across the mandibular canal with a constriction of the mandibular canal as it passes through the roots; thus, the canal has an hourglass appearance.

The mandibular canal develops in the mandible many years prior to the development of the third molar. Thus, as the roots of the third molar develop in relation to the canal, they may contact the bony wall of the mandibular canal, and as they grow they may partially or completely encircle it (Fig. 4). Often a groove is formed on the side of the root where it contacts the canal during the developmental period of the root (Fig. 2).

Fig. 2.—Both roots extend below the mandibular canal. A groove was visible on the lateral aspect of the roots following removal of the tooth.

Fig. 3.—The mandibular canal appears constricted where it passes between the roots.

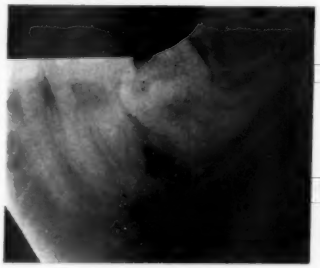

Fig. 4.—The mesial aspect of the roots, as a result of the distal curvature, is in close proximity to the mandibular canal; it exhibited a groove when viewed after extraction.

Occasionally a small fragment of tissue from the canal will remain attached to the tip of a curved root, resulting in anesthesia of the area innervated by the inferior alveolar nerve distal to the area of injury (Fig. 5).

Teenage patients often exhibit contact of developing third molar roots with the mandibular canal (Fig. 6). This relationship does not often result in disturbance of the canal during extraction. However, such relationships may result in referred pain during the periods of rapid root growth.

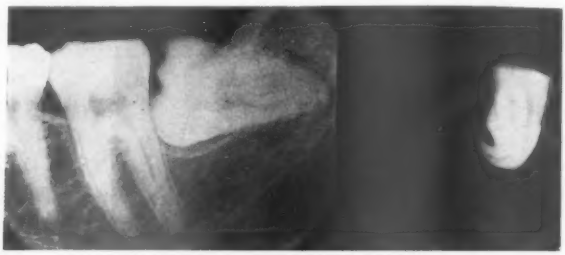

Fig. 5.—Small fragment of tissue adherent to tip of curved root determined by microscopic examination to be nerve tissue.

Fig. 6.—Developing third molar roots adjacent to the mandibular canal.

The appearance of these diagnostic factors in the roentgenogram suggests the type of surgical procedure necessary, as well as the need for forewarning the patient of the possibility of postoperative paresthesia or anesthesia. The operator who carefully plans his surgical procedure can usually complete the operation satisfactorily without damage to the contents of the canal.

ENDODONTICS

The American Association of Endodontists

Victor H. Dietz, Editor

BACTERIOLOGIC RESULTS FROM 4,000 ROOT CANAL CULTURES

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INTRODUCTION

THE root canal culture is, in the first place, a test for sterility. Consequently, it is of use only if careful aseptic and endodontic techniques are practiced. Aseptic technique is, nevertheless, requisite to endodontic treatment. If only as a check on aseptic technique, root canal culture is of important educational value.

The results of culturing depend partly on the medium used for primary culture.[7, 11, 14, 16] In a previous publication,[1] we compared various media. Brain-heart infusion with 0.05 per cent agar in screw-capped bottles proved quite satisfactory and permitted the growth of most common aerobic and anaerobic organisms.

Whether or not the root canal culture gives a true picture of the bacteriologic situation in the canal has been much discussed. It has been claimed, on the basis of theoretical considerations, that a negative culture from a positive canal would be a regular occurrence. Many authors, therefore, require two consecutive negative cultures before they will accept sterility of the canal.[5, 8, 15] Van Amerongen[2] showed, however, that with a suitable technique the probability for a positive culture after one or after two negative cultures is equal and low (2 to 3 per cent for experienced operators; 8 to 9 per cent for students). The probability that the canal is sterile is not higher after two negative cultures than after one negative culture. Furthermore, large masses of dentine filed from the wall of a well-prepared canal generally were sterile if the normal paper-point culture had been sterile, giving further proof that negative cultures from root canals are representative in practice. The number of false positives is fairly high, of course, but it decreases with experience in aseptic techniques.[2, 9]

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A high percentage of infected canals become sterile by mechanical preparation of the root canal.[6, 17] In our experience, this percentage was 64 per cent.[3] This phenomenon stresses the view that what you take out of the canal is at least as important as what you put into it. In this connection, a comparison was made of the results obtained with chlorophenol-camphor-menthol and polyantibiotics.[4] The results showed that although the number of applications necessary to obtain sterility was slightly smaller in the group treated with polyantibiotics, the mean number of sessions was equal in both groups.

Regular culturing from root canals, starting with an initial culture during the first session, reduces the number of sessions necessary for treatment. The culture provides an invaluable check on the careful aseptic technique which is required for good root canal treatment. Without this regular check (that is, with less careful technique), the number of infected canals becoming sterile by preparation alone would be much less than 64 per cent. This leads to the remarkable paradox[2] that root canal cultures are important for those who do not practice them and much less so for those who do. That a sound knowledge of the bacterial flora in infected canals is of importance in cases where focal infection is considered needs no comment.

Having advocated the practice of root canal cultures, we wish to report on the bacteriologic results of more than 4,000 cultures from more than 1,000 canals.

MATERIALS AND METHODS

Endodontic Techniques.—These have been described before.[1] After extensive mechanical cleansing of the exterior of the tooth, the rubber-dam was applied (when necessary, after insertion of a temporary inlay). The tooth in question was disinfected by the application of 5 per cent tincture of iodine. After the removal of all carious dentine this disinfection was repeated. The roof of the pulp chamber and the coronal pulp were then removed with sterile instruments; they were flushed repeatedly with sterile saline. For initial cultures, a sterile paper point was brought in contact with the contents of the canal. For initial cultures from cases of old endodontic treatments, periapical secretion was collected and dentine particles were filed from the canal wall. After mechanical preparation, some dentinal material was filed from the wall of the dry canal and a paper point was introduced, care being taken to make contact with the periapex. The paper point was left in situ for three minutes, wet with sterile saline, and transferred to the culture bottle. After the application of drugs, the canal was washed with 2 ml. of sterile saline. It has been shown[1] that this technique prevents growth inhibition of the used medicaments.

Most cultures were taken by advanced dental students; a number of cases were treated by experienced dentists on the staff of our dental school.

Bacteriologic Procedures.—Primary cultures were taken in screw-capped 5 ml. bottles filled with brain-heart infusion broth (Difco) to which 0.05 per

cent of agar had been added (B.H.I.) All cultures were incubated at 37° C. As soon as turbidity was observed, a microscopic preparation was made and the fluid was subcultured on three (later four) solid media. One blood agar plate was incubated aerobically. One blood agar plate and a Rogosa medium (pH 6.8) were incubated anaerobically. A Chapman plate, incubated aerobically, was added at a later period. In many cases these plates showed pure cultures. From the colony form and stained slides, a rough classification could be made. This was then confirmed, depending on the case, by short sets of biochemical tests or by serologic tests. From mixed infections, different colonies were picked and subcultured for further identification.

Identification was, of necessity, preliminary. Important strains were kept for further study. With growing experience, it became possible (even with simple means) to allot each isolated strain to a definite group.

It is recognized that in the fluid primary culture some organisms might be selected and others suppressed. To arrive at more quantitative results, we plated the paper points directly and in another series triturated the paper points in broth with sterile sand and plated the resulting fluids. As neither of these experiments was encouraging, we adhered to the technique described.

The properties used for identification of the isolated strains will be described with each organism. Serologic grouping of streptococci was accomplished by Fuller extraction and precipitation in capillary tubes with commercial sera.

During a certain period of the study the value of two different culture media for primary culture was studied by taking duplicate cultures from each canal. It has been shown before[1] that duplicate cultures very often give equal results and that there is only slightly more chance for a positive culture from the first point than from the second. One paper point was cultured in brain-heart infusion, the other in brain-heart infusion to which 0.1 per cent of glucose was added. (The commercial product contains a very small amount of glucose.) The order of these two cultures was alternated. The results are given in Fig. 1.

B.H.I. / B.H.I. + glucose	+	−	
+	107	29	136
−	21	224	245
	128	253	381

Fig. 1.

There seems to be a slight tendency toward B.H.I. plus glucose, which for this small number, of course, is not significant. From the 107 doubly positive cultures, the cultures with glucose showed growth at an earlier time in ten cases. The reverse was true in six cases. There was no obvious difference between the species of organisms cultured on the two media.

Since January, 1958, all primary cultures were made in B.H.I. plus glucose. A definite increase in the frequency of lactobacilli from 2 to 8 per cent was observed after that time. There was possibly also a slight increase in *Streptococcus salivarius* but this may have been due to chance. The increased frequency of lactobacilli is obviously due to the improved growth conditions for this organism in the medium with glucose.

RESULTS

Survey of Flora From All Cultures.—

A total of 4,186 cultures were taken. Of these, 2,989 cultures (72 per cent) were negative and 1,141 (27 per cent) were positive. The frequency distribution of the isolated organisms is given in Table I and Fig. 2. For details, the footnote to Table I should be consulted. In 903 cases one organism was isolated, whereas 238 cultures (21 per cent) contained more than one organism (mixed infections).

TABLE I. STRAINS ISOLATED FROM 4,186 ROOT CANAL CULTURES

ORGANISM	A IN PURE CULTURE	B IN MIXED INFECTIONS	C TOTAL	D NUMBER OF TEETH	E Q = C/D
Streptococcus faecalis	240	45	285	138	2.07
Streptococcus mitis	153	130	283	200	1.42
Streptococcus salivarius	5	15	20	19	1.05
Streptococcus hemolyticus	33	22	55	33	1.67
Anaerobic streptococcus	54	15	69	41	1.69
Indifferent streptococcus	81	71	152	95	1.60
Other streptococci	11	17	28	26	1.08
Total	577	315	892	552	1.62
Micrococci	161	71	232	177	1.32
Lactobacilli	57	41	98	65	1.51
Diphtheroids	45	13	58	48	1.20
Gram-positive rods	10	11	21	15	1.40
Bacillus species	9	12	21	17	1.24
Actinomyces	17	3	20	18	1.11
Fusiformis	5	3	8	7	1.14
Sarcina	1	—	1	1	—
Neisseria	1	14	15	13	1.16
Gram-negative rods	5	23	28	27	1.03
Yeasts	15	8	23	18	1.28
Mixed infection	238				
Total positive cultures	1,141	Total organisms 1,417			
Turbid, no growth	56				
Negative cultures	2,989				
Total	4,186				

In fifty-six cases (1.5 per cent of all cultures) a slight turbidity, which could not be subcultured, was observed.

In column B the frequency of any organism in mixed infections is given. As each mixed infection contributes at least two organisms, the total number of organisms (sum of column C) is appreciably higher than the total number of positive cultures.

Column D gives the number of teeth from which the strains of each group (column C) were isolated. The last column gives the total number of each organism divided by the number of teeth from which they were isolated. This ratio is a measure of the number of times the same organism was isolated from one canal. Organisms with a high ratio seem able to persist longer in the canal. (The ratio was not corrected for the number of teeth with more than one canal.)

The preponderance of streptococci (51 per cent of pure cultures, 63 per cent of all organisms) is obvious. Micrococci, with 14 per cent, and lactobacilli, with 8.5 per cent, are next in number. Neisseria and *Streptococcus salivarius,* though abundant in the mouth, are rare and occur mainly in mixed infections (Table I, column 2), which probably means that they cannot maintain themselves in the root canal. For the same reason, gram-negative rods are considered secondary invaders.

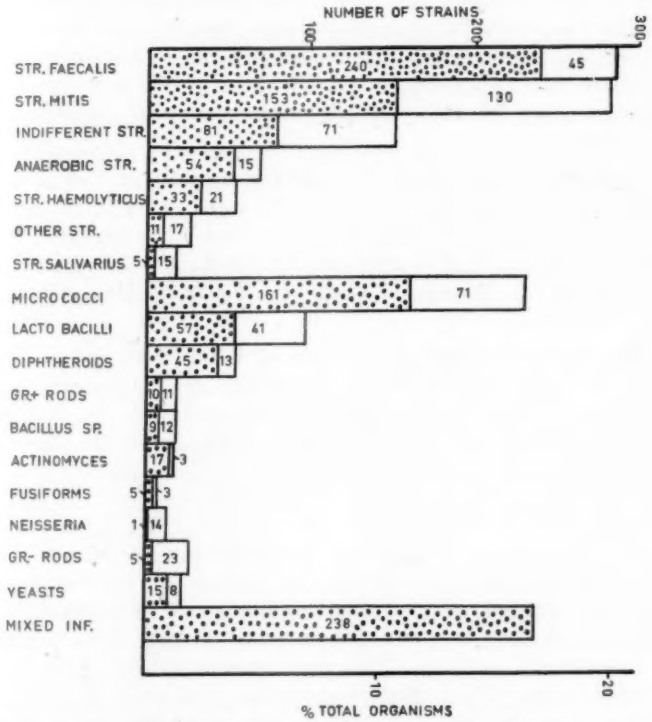

Fig. 2.—Frequency distribution of strains in 1,141 positive cultures. Shaded columns represent strains in pure culture; white columns represent additional strains from mixed infections. The per cent scale at the right refers to all organisms (shaded and white columns together). The shaded columns cannot be referred to this scale (see Table I).

Streptococcus faecalis: All strains presented under this heading showed characteristic large α-hemolytic colonies. All strains withstood heating for 30 minutes at 60° C.; they fermented mannitol and esculin. Most strains were slightly more bile sensitive than the usual fecal strains.[13] Many strains were grouped serologically; they were always group D.

The strains mentioned as *Streptococcus faecalis* in the table include *Streptococcus liquefaciens.* During a certain period of the study, all strains were classified in this respect. Thus, from July, 1957, to July, 1958, 158 strains of

D streptococci were cultured (144 pure cultures, 14 from mixed infections), from which fifty-nine liquefied gelatin (37 per cent). *Streptococcus faecalis* was often isolated more than once from one canal (mean ratio, 1.89). For *Streptococcus liquefaciens*, this ratio was 2.96, which means that *Streptococcus liquefaciens* persists much longer in root canals than any other organism.

Streptococcus mitis: All α-hemolytic strains that could not otherwise be classified are presented under this heading. None of them produced slime from saccharose on solid medium. All strains that were tested serologically proved ungroupable; some strains were tested with Optochin and proved insensitive. During a certain period, a subdivision by colony form and fermentation reactions was attempted but appeared useless. Twenty randomly selected strains were tested for collagenase by incubating with Azocol[12]; only one strain was positive.

Streptococcus hemolyticus: From the fifty-five strains, forty-nine were grouped serologically. Twenty-eight (57 per cent) were group F, fifteen (30 per cent) were group G, two were group C, and four were not groupable with the available sera. Groups F and G were often isolated more than once from one patient (ratio about 2). For group C and the nongroupable strains, this ratio was 1.

Indifferent streptococci: These strains formed minute colonies on blood agar and did not show any change in the blood medium. All strains were insensitive to Optochin. They generally grew better anaerobically, and consequently the group merged with the next. In the beginning of the study, no classification was attempted. Later, the strains were tested serologically after Fuller extraction. From a series of forty strains, twenty-three reacted with the available sera: group F, ten; group G, six; group C, four; group D, two; and group E, one. Guthof[10] and Wensinck[19] described analogous observations. All groupable strains fermented glucose, lactose, saccharose, maltose, salicin, and trehalose but not raffinose, arabinose, mannitol, sorbitol, or amylum. Lactose fermentation occasionally was retarded. Five of the ungroupable strains had the same fermentation pattern. The other ungroupable strains showed slightly different patterns. These facts point to a relationship between the groupable indifferent strains and hemolytic strains with the same cell-wall antigen. Ten indifferent strains were subcultured daily for several weeks in blood broth; none became hemolytic. The strains are under study and will be reported upon later. A relationship between these indifferent strains and hemolytic streptococci of groups C, G, and F might be important with respect to problems of focal infection and endocarditis.

Indifferent anaerobic streptococci: None of these strains showed α or β hemolysis; they were completely indifferent toward blood. Judged by the (limited) fermentation tests described by Weinberg and associates,[18] many of these strains could be described as *Streptococcus micros* and some others seemed to belong to *Streptococcus intermedius*. A large number of these strains were groupable. Of a series of ten strains, seven belonged to group C.

The fermentation patterns of these group C streptococci were equal to those of the former group, although three of the anaerobic strains did not ferment trehalose.

Although the evidence is incomplete, there seem to be many indications that the hemolytic, indifferent, and indifferent anaerobic streptococci isolated here are in some way related. That there exist other reasons to consider them as one group will be shown below.

Other streptococci: All the strains mentioned under this heading in Table I were α hemolytic. Some differed in colony form from the usual *Streptococcus mitis.* Some strains were scored as *Streptococcus mitis* and lost before further study; others remained completely unidentified. The whole group should probably be added to the mitis category.

Lactobacilli: Lactobacilli were rare (2 per cent of all organisms) during the first part of the investigation. Following the introduction of brain-heart infusion with glucose as primary culture medium, their number increased (8 per cent). Judging from the colony form on Rogosa medium, the strains were mainly *Lactobacillus casei* (or *plantarum*). Twelve strains were further identified. Of those, nine were *Lactobacillus casei,* one was *L. fermenti,* and one was *L. plantarum.*

Mixed infections: Of 196 mixed infections, 173 contained two organisms, and 20 contained three organisms; four organisms were cultured twice, and once five organisms were cultured. Among the double combinations *Str. faecalis* was found thirty-one times, *Str. mitis* 100 times, indifferent streptococci twenty-three times, micrococci eight times, and *Str. hemolyticus* ten times. Among the triple combinations, *Str. faecalis* was present eight times, and *Str. mitis* was present ten times.

Micrococci: Twice, a coagulase positive *Micrococcus pyogenes* was isolated. All other isolated strains showed white colonies on blood agar. All were anhemolytic and coagulase-negative. It will be argued below that the bulk of these strains are due to chance contaminations.

Bacterial Flora From Different Clinical Situations.—

There were complete case histories from 902 patients (canals). These involved 3,312 cultures, of which 993 (30 per cent) were positive. A slight turbidity in the primary culture which could not be subcultured (T.N.G. = turbid, no growth)* was present in thirty-six cases. There were 2,317 (70 per cent) negative cultures.

The complete data, differentiated for vital pulps, open or closed necrotic pulps, and old endodontic cases, are given in Table IIA for initial cultures and in Table IIB for later cultures. Some details are discussed in the footnote to these tables. In Table III a summary is given, and it is convenient to discuss this table only.

*Possibly abundant blood from pulp.

TABLE IIA. FREQUENCY OF ORGANISMS IN INITIAL CULTURES

ORGANISM	VITAL PULPS			OLD CANAL TREATMENTS			OPEN NECROTIC PULPS			CLOSED NECROTIC PULPS		
	P	T	PER CENT	P	T	PER CENT	P	T	PER CENT	P	T	PER CENT
1. *Streptococcus faecalis*	27	35	15	7	11	13	3	6	8	18	25	19
2. *Streptococcus mitis*	42	68	29	12	23	28	10	21	29	24	37	28
3. *Streptococcus salivarius*	1	2	1	0	2	2	0	5	7	1	1	1
4. *Streptococcus hemolyticus*	2	3	1	0	1	1	1	5	7	2	4	3
5. Anaerobic streptococci	2	5	2	5	5	6	0	1	1	3	3	2
6. Indifferent streptococci	6	15	6	5	9	11	2	8	11	5	16	12
7. (4 + 5 + 6)		23	10		15	18		14	19		23	17
8. Total streptococci		128	55		51	62		46	64		86	65
9. Micrococci	22	39	17	6	12	14	2	7	10	7	12	9
10. Lactobacilli	9	12	5	8	8	9	0	6	8	3	8	6
11. Diphtheroids	17	22	9	4	4	5	2	4	6	6	9	7
12. Bacillus species	1	3	1	0	3	3	-	-		1	3	2
13. Actinomyces	1	1	-	-	-		1	3	5	2	2	1
14. Fusiformis	-	-		-	-		-	-	-	1	2	1
15. Neisseria	0	5	2	-	-		0	2		-	-	
16. Gram-negative rods	-	-		1	4	5	0	2		0	2	1
17. Yeasts	7	10	4	1	1	1	1	1		0	1	1
18. T.N.G.	13	13	6	-	-		1	1		7	7	5
19. Subtotal	150	233	100	49	83		23	72		80	132	
20. Mixed infections	42		9	15		8	16		36	31		14
21. Total positive cultures	192		41	64		38	39		89	111		51
22. Negative cultures	279		59	105		62	5		11	107		49
23. Total cultures	471		100	169			44			218		

In each column the first figure refers to the number of strains present in pure culture (P); the second gives the total number of times strains of that denomination were isolated (T). The number of strains occurring in mixed infections is equal to the difference between T and P. The last figure in each column gives the frequency of the "species" as a percentage of the total number (line 19). Below the double horizontal line, percentages are given in terms of the total number of cultures.

The results for all necrotic pulps (the sum of columns 2, 3, and 4) are given in Table III.

The number of cases of old canal treatments and open necrotic pulps is small. In some cases it is hardly enough to permit calculation of percentages.

In old canal treatments anaerobic streptococci are high in initial cultures (Table IIA, line 5), but this is not true for later cultures (Table IIB, line 5).

In open necrotic pulps *Streptococcus faecalis* is infrequent (line 1, both tables). Hemolytic streptococci are frequent (line 4, both tables). The whole group of anaerobic, indifferent, and hemolytic streptococci in later cultures is very frequent (Table IIB, line 7). These organisms seem the best settlers compared with the rest of the oral flora.

O. S., O. M. & O. P. July, 1959

TABLE IIB. FREQUENCY OF ORGANISMS IN LATER CULTURES

ORGANISM	VITAL PULPS			OLD CANAL TREATMENTS			OPEN NECROTIC PULPS			CLOSED NECROTIC PULPS		
	P	T	PER CENT	P	T	PER CENT	P	T	PER CENT	P	T	PER CENT
1. *Streptococcus faecalis*	53	62	21	24	24	28	4	5	9	53	58	23
2. *Streptococcus mitis*	29	56	19	5	9	10	8	13	22	30	51	20
3. *Streptococcus salivarius*	2	6	2							1	2	0.8
4. *Streptococcus hemolyticus*	1	4	1	1	1	1	7	13	22	13	13	5
5. Anaerobic streptococci	9	10	3	1	3	3	2	4	7	20	23	9
6. Indifferent streptococci	21	31	11	8	11	13	9	11	19	9	15	6
7. 4 + 5 + 6		45	15		15	17		28	48		51	20
8. Total streptococci		169	58		48	55		36	62		162	64
9. Micrococci	52	72	25	15	16	18	4	4	7	30	39	15
10. Lactobacilli	8	16	5.5	10	12	14	0	3	5	6	13	5
11. Diphtheroids	7	11	4	3	4					8	10	4
12. Bacillus species	5	6	2	0	1					2	4	2
13. Actinomyces	2	2	1	1	1					4	4	2
14. Fusiformis										2	6	2
15. Neisseria				0	2					0	4	2
16. Gram-negative rods		1		1	2					2	2	1
17. Yeast	6	9	3				0	1		1	1	
18. T.N.G.	3	3	1	1	1		2	2		9	9	3
19. Subtotal	198	289		70	87		38	58		190	254	
20. Mixed infections	43		4	8		2	8		6	32		5
21. Total positive cultures	241		20	78		18	46		32	222		34
22. Negative cultures	934		80	348		82	98		68	441		66
23. Total cultures	1,175		100	426			144			663		
24. Patients (canals)	471			169			44			218		

TABLE III

ORGANISM	INITIAL CULTURES				NOT INITIAL CULTURES				ALL CULTURES		ALL CULTURES		TOTAL	
	I (VITAL)		II (NECROTIC)		III (VITAL)		IV (NECROTIC)		V (VITAL)	VI (NECROTIC)	VII (INITIAL)	VIII (NOT INITIAL)	IX	
	NUMBER	PER CENT	NUMBER	PER CENT	NUMBER	PER CENT	NUMBER	PER CENT	PER CENT	PER CENT	PER CENT	PER CENT	NUMBER	PER CENT
1. *Streptococcus faecalis*	35	15	42	15	62	21	87	22	19	19	15	22	226	19
2. *Streptococcus mitis*	68	29	81	28	56	19	73	18	24	22	29	19	278	23
3. *Streptococcus salivarius*	2	1	8	3	6	2	2	0.5	1	1	2	1	18	1
4. *Streptococcus hemolyticus*	3	1	10	3	4	1	27	7	1	5	2	4	44	4
5. Anaerobic streptococci	5	2	9	3	10	3	30	7	3	6	3	6	54	4
6. Indifferent streptococci	15	6	33	11	31	11	37	9	9	10	9	10	116	10
7. 4 + 5 + 6	23	10	52	18	45	15	94	24	13	21	14	20	214	18
8. Streptococci total	128	55	183	64	169	58	256	64	57	64	60	61	736	61
9. Micrococci	39	17	31	11	72	25	59	15	21	13	13	19	201	17
10. Lactobacilli	12	5	22	7	16	5	28	7	5	7	6	6	78	6
11. Diphtheroids	22	9	17	6	11	4	16	4	6	5	7	4	66	5
12. Other organisms	19	8	26	9	18	6	28	7	7	8	9	7	91	7
13. T.N.G.	13	6	8	3	3	1	12	3	3	3	4	2	36	3
14. Total	233	100	287	100	289	100	399	100	–	–	–	–	1,208	100
15. Cultures with streptococci	116	25	151	35	154	13	235	19	16	23	30	16	656	20
16. Cultures with micrococci	39	8	31	7	72	6	59	5	7	5	8	5	201	6
17. Total positive cultures	192	41	214	50	241	20	346	28	26	34	45	24	993	30
18. Negative cultures	279	59	217	50	934	79	887	72	74	66	55	76	2,317	70
19. Total cultures	471		431		1,175		1,233						3,310	

In each column the first row gives the number of strains of the indicated "species" which were isolated. The second row gives the frequency of each organism as a percentage of the total number of organisms, including T.N.G. (line 14). In columns V to VIII the first row is omitted. The omitted numbers are the sums of the numbers in columns I + III, II + IV, I + II, and III + IV, respectively.

Line 8 gives the frequency of all streptococci; line 7 gives the frequency of the hemolytic, indifferent, and indifferent anaerobic streptococci, which in several respects can be considered as one group.

Below the double horizontal line the percentages are given in terms of the total number of cultures (line 19).

The last column (IX) lists the frequency of each organism as percentage of the total number of organisms isolated. *Streptococcus faecalis* was present in 19 per cent, *Streptococcus mitis* in 23 per cent, and micrococci were present in 17 per cent. There is again a definite preponderance of streptococci, which form 61 per cent of all organisms (line 8) and occur in 20 per cent of all cultures (line 15).

Comparing initial cultures with later cultures, we find that the percentage of positive cultures is much higher among the initial cultures (45 per cent, column VII, line 17) than among later cultures (24.3 per cent, column VIII). As the cultures were taken at different stages of preparation and from all canals until one negative culture had been obtained (including one control culture immediately before filling which generally was negative[1]), this preponderance of negatives among later cultures is obvious.

If one is to understand the meaning of the frequency distribution of different organisms in the cultures, some theoretical considerations seem necessary.

The origin of the cultured bacteria is obviously of different kinds:

1. If we consider the procedure for taking initial cultures from accidentally exposed sound pulps, it is obvious that even with the strictest technique the chances of carrying bacteria of the carious cavity into the pulp during perforation of the roof of the pulp chamber are large. Contamination with salivary organisms through leaky rubber-dams should also be considered. This means that the number of positive cultures from pulps that did not contain bacteria before preparation will be large. In these cases the number of bacteria will probably be relatively small. As for the kind of organisms one may expect, all organisms that can be present in the deep carious lesion. If the mechanical preparation of the root canal does not immediately follow exposure of the pulp, some of these organisms might establish a clinical infection.

2. In the case of actual infection of the root canal, as in pulpitis and most cases involving necrotic pulps, the causal organism will nearly always have penetrated into the pulp from the carious lesion. Not all organisms will be able to maintain themselves in the pulp; only a small fraction of the caries flora will be able to overcome the natural defense of the living pulp. In infected and in necrotic pulps one may consequently expect a much smaller number of species, but the species that establish themselves will be present in relatively large numbers (unless the lesion has "sterilized" itself).

3. Finally, the chance contamination of the culture from the air, from instruments, or from the hands of the operator indirectly is to be considered.

Differences Between Flora From Vital and Necrotic Pulps.—From the difference between the flora from vital and necrotic pulps, it would seem easy to

decide which organisms were possible pathogens and which were chance contaminants. The difficulty is that the chance contamination during the opening of the canal is superimposed on the flora of the infected canal. Only quantitative evaluation of the number of bacteria of different species in the sample would permit a distinction between the cases mentioned under 1 and 2 above. With the present technique, any chance contaminant will grow in the fluid primary culture and confuse the issue.

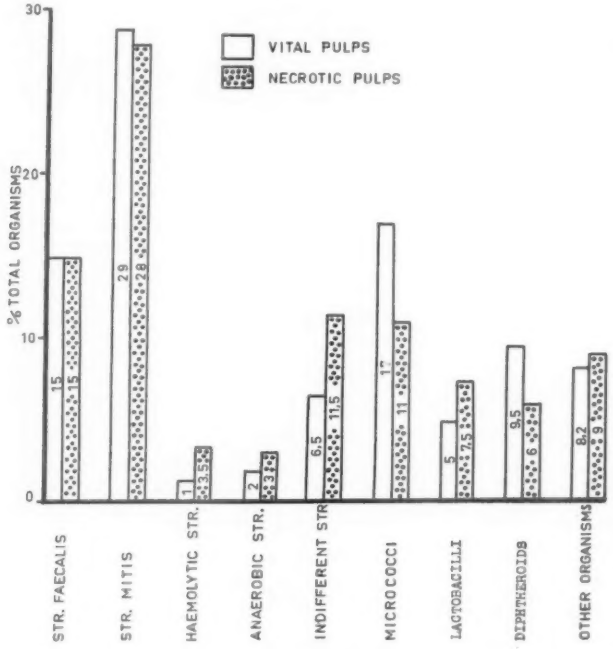

Fig. 3.—Frequency distribution of strains in initial cultures. The hemolytic, anaerobic, and indifferent streptococci and the lactobacilli occur with increased frequency in necrotic pulps. All other organisms are less frequent in necrotic than in vital pulps or show equal frequencies.

Nevertheless, some indications concerning an eventual pathogenic significance of some species might be obtained by comparing cultures from exposed sound pulps with those from necrotic pulps (Table III). On comparison of columns I and II, III and IV, and V and VI (line 17), it can be seen that the percentage of positive cultures from necrotic pulps is higher (41 to 50 per cent for initial cultures, $p < 0.05$, for the other differences $p < 0.01$). No large differences in the flora seem to exist. However, there is a definite increase in the percentage of streptococci (line 8), mainly due to the groups of hemolytic, anaerobic, and indifferent streptococci (Table III, line 7; 10 to 18 per cent for initial, 15 to 24 per cent for later, and 13 to 21 per cent for all cultures, all

$p < 0.05$; compare also Figs. 3 and 4). This seems to point to a possible role for these organisms as primary invaders. *Streptococcus mitis* is equally frequent in all cases.

The group of micrococci appears to be found in a fairly constant percentage of all cultures in all groups (Table III, line 16; only the difference between columns VII and VIII has a $p < 0.05$). If calculated as percentage of all organisms (line 9), the micrococci are less frequent in cultures from necrotic pulps (21 → 13 per cent columns V and VI; $p < 0.01$). This is obviously due to the higher percentage of positive cultures from necrotic pulps. They are also less frequent in initial cultures than in later cultures (line 9, columns VII and VIII). This, again, is due to the higher frequency of negatives among the

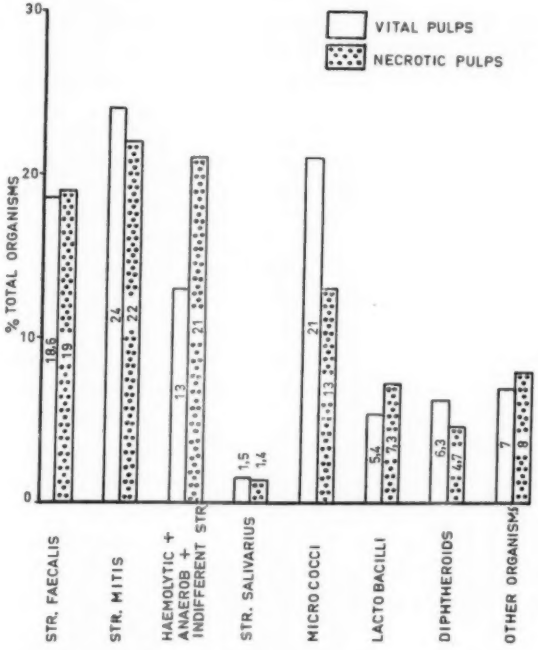

Fig. 4.—Frequency distribution of strains in all cultures. The group of hemolytic, anaerobic, and indifferent streptococci occurs with increased frequency in cultures from necrotic pulps.

later cultures. This seems to indicate that they are mainly chance contaminants. This view is supported by the fact that only coagulase-negative micrococci (abundant on human skin) were found. The point is further stressed by the much lower percentage of staphylococci found in cultures taken by experienced dentists than in those taken by students (Table IV).

Organisms Persisting in the Root Canal.—In comparing the flora of initial cultures with that of later cultures, one might acquire some information about

TABLE IV. FREQUENCY OF MICROCOCCI IN CULTURES FROM EXPERIENCED DENTISTS AND STUDENTS

CULTURE	DENTISTS		STUDENTS	
	NUMBER	PER CENT	NUMBER	PER CENT
Cultures with micrococci	17	2.5	184	7
Cultures with streptococci	133	20	523	20
Cultures with other bacteria	26	4	144	5.4
Positive cultures	172	26	821	31
Negative cultures	493	74	1,824	69
Total	665		2,645	
Micrococci (per cent from positive cultures)		10		22

The sum of the cultures with micrococci, streptococci, and other bacteria is not equal to the number of positive cultures, as there were four mixed infections with micrococci and streptococci in the dentist group and twenty in the student group.

The most experienced dentist had 1.8 per cent cultures with micrococci; the other 3.5 per cent.

the organisms that are able to persist in the root canal. On comparison of columns I and III, II and IV, and VII and VIII (Table III), there seem to be no large differences. This is due again to the large background of chance contaminations. Studied more closely, however, it appears that *Streptococcus faecalis* is present more frequently in later cultures (15 to 22 per cent, line 1, columns VII and VIII). The same is true for hemolytic, anaerobic, and indifferent streptococci (14 → 20 per cent, line 7). *Streptococcus mitis* is less

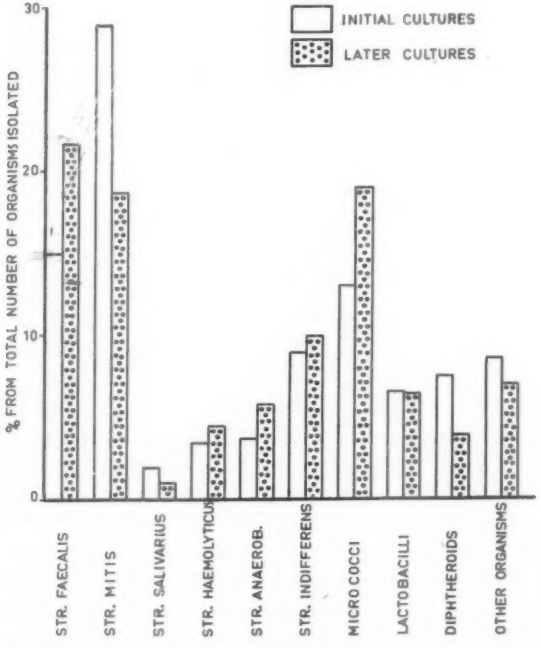

Fig. 5.—Frequency distribution of strains in all cultures. Organisms that persist in the root canal will be present with higher frequency in later cultures. These are *Streptococcus faecalis*, the hemolytic, anaerobic, and indifferent streptococci. The apparent increase of micrococci is due to other causes (see text).

frequent in later cultures. *Streptococcus faecalis, Streptococcus hemolyticus,* and the anaerobic streptococci seem to persist better in the root canal than do other organisms (Fig. 5).

Another approach to the possible role of the isolated strains in root canal infection is the study of cases in which the same organism was isolated more than once from the same canal. This was performed by counting the cases in which the organism found in the first culture was again found (consecutively) in the second, third, etc., cultures from the same canal. In the cultures from vital pulps there were forty-three (24 per cent) such cases where an organism was found more than once. In the group from necrotic pulps this number was eighty (39 per cent). The distribution of organisms is given in Table V.

In some cases the numbers seem small. It should be remembered, however, that the probability for a consecutive series of three cultures of, for example, *Streptococcus hemolyticus* is extremely small (compare note under Table V). It is obvious that some organisms persist whereas others do not (Table V, last three columns). The organisms that persist longest (that is, maintain themselves best) seem to be *Streptococcus hemolyticus, Streptococcus faecalis,* indifferent streptococci, indifferent anaerobic streptococci, and perhaps lactobacilli and *Streptococcus mitis.* All other organisms are present only in the initial cultures, and as they disappear after preparation they do not seem to have settled themselves in the dentine or in the periapical tissues. The separate results for vital and necrotic pulps are given in the first half of Table V. Long series of consecutive cultures occur mainly in the group with necrotic pulps. For *Streptococcus faecalis, Streptococcus hemolyticus,* the indifferent streptococci, and lactobacilli, the percentage of consecutive positives is higher in the cultures from necrotic pulps. This is not so for micrococci and *Streptococcus mitis;* consequently, we consider these organisms as less important.

In many cases given as consecutive series of cultures of *Streptococcus faecalis,* it was definitely *Streptococcus liquefaciens* which was isolated. If we divide the number of times *Streptococcus liquefaciens* was isolated by the number of all canals in which *Streptococcus liquefaciens* was found, the ratio is 3, as has already been discussed. As the ratio for *Streptococcus faecalis* is only 2, there is no doubt that *Streptococcus liquefaciens* persists better in the root canal than *Streptococcus faecalis.*

The fact that long series of consecutive cultures positive for one organism can occasionally be obtained from vital pulps requires explanation. Apart from the obvious difficulty in clinical diagnosis, we think that in some of these cases a contamination during opening of the canal could have established itself as a clinical infection in the period between instrumental entry and mechanical preparation (generally one week).

In an analogous calculation the cases with more than one culture with the same organism were counted but the requirement of consecutiveness was omitted. The results pointed in the same direction. The number of cases was somewhat larger. The order of the organisms, in terms of frequency of three or more

TABLE V. NUMBER OF CANALS SHOWING THE SAME ORGANISM MORE THAN ONCE CONSECUTIVELY

ORGANISM	VITAL PULPS						NECROTIC PULPS						VITAL + NECROTIC		
	+ – –	++–	+++	++++ AND +++++	TOTAL	PER CENT ++ OR MORE	+ – –	++–	+++	++++ AND +++++	TOTAL	PER CENT ++ OR MORE	TOTAL	PER CENT ++ OR MORE	PER CENT +++ OR MORE
Streptococcus faecalis	17	10 (2)*	—	4	31	45	12	11 (3)	8	7	38	68	69	58	27
Streptococcus hemolyticus	2	—	—		2	0	2	2 (0.2)	—	4	8	75	10	60	40
Anaerobic streptococci	2	1 (0.05)	1	1	5	(60)	5	4 (0.02)	1	1	11	55	16	56	25
Indifferent streptococci	9	3 (0.5)	—	1	13	31	10	8 (1)	7	—	25	60	38	50	21
Streptococcus mitis	45	12 (3)	3	—	60	25	44	10 (5)	3	1	58	24	118	29	6
Micrococci	24	4 (2.3)	1	—	29	17	19	3 (1.5)	1	—	23	17	52	17	4
Diphtheroids	16	—	—	—	16	0	15	—	1	1	17	12	33	6	6
Lactobacilli	9		1	—	10	10	5	5 (0.5)	1	1	12	58	22	36	13
Others	11	1	—	—	12	8	12	—	—	—	12	0	24	4	0
Total	135	31	6	6	178	24	124	43	22	15	204	39	382	33	13

*The numbers in parentheses in the columns ++– refer to the frequency for two consecutive positive cultures expected from chance alone.

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positive cultures from one patient, was again *Streptococcus faecalis, Streptococcus hemolyticus, anaerobic streptococci, indifferent streptococci,* lactobacilli, *Streptococcus mitis* and micrococci.

DISCUSSION

The chance of carrying bacteria from the carious cavity into the root canal during the opening of the canal is relatively great. Consequently, a large fraction of root canal cultures, even those from exposed sound pulps, will be positive due to this type of contamination. The large background of chance contamination hampers the analysis of results. This large background is due partly to the fact that most cultures discussed in this article were taken by relatively inexperienced operators. The study of an equally large amount of material gathered by experienced dentists would be much more useful.

Another serious difficulty in the interpretation of results is the fact that the primary culture had to be made in fluid medium, in which some organisms will have been selected and others suppressed. Development of a method for a more quantitative evaluation of the root canal flora is obviously of great importance. Until such a method has been developed, it will be difficult to arrive at definite conclusions concerning the pathogenic importance of the isolated organisms.

Recognizing these limitations, however, we believe that an analysis of the available results permits some tentative conclusions.

The coagulase-negative micrococci, which form 17 per cent of all organisms, are to be considered as chance contaminants. Irrespective of the conditions of the canal or the stage of treatment, they occur with equal frequency in all cultures. Expressed as a fraction of total organisms, they are less frequent in infected pulps than in sound pulps. The number of two consecutive cultures with micrococci from one canal does not differ greatly from the number expected from chance alone (Table V). Furthermore, there is a definite negative correlation between the frequency of micrococci and the technical skill of the operator (Table IV).

For *Streptococcus mitis* the data are much less definite. This organism might also be a chance contaminant, as it occurs with equal frequency in cultures from vital and from necrotic pulps and is less frequent in later cultures (Table III). The number of consecutive cultures with *Streptococcus mitis* from one canal is equal for vital and for necrotic pulps (Table VI) and, although it is larger than from chance alone, the difference is much less than for any other organism (except micrococci). As the group called *Streptococcus mitis* is probably heterogeneous, it is quite possible that it still contains a fraction of possible pathogens. A large fraction are probably chance contaminants, however, as was to be expected from the organism's abundance in the mouth.

Among the other streptococci, the hemolytic indifferent and anaerobic indifferent streptococci seem to be serious candidates for a possible role as the cause of pulp infections. The same seems to be true for the group D streptococci, although the evidence is less unequivocal here.

The hemolytic, indifferent, and anaerobic indifferent streptococci can be treated as one group because, irrespective of the differences in oxygen requirement and hemolysis, they show relationships in cell-wall antigens and fermentation patterns. In the future, it would be better perhaps to give priority to the serologic character and discuss the significance of F, G, and C streptococci separately. At the moment, we will take the whole group together.

As they are more frequent in cultures from necrotic pulps than from vital pulps (Figs. 2 and 3), more frequent in later than in first cultures, have a high mean ratio of cultures per canal (Table I), and occur more often in consecutive series of positive cultures from one canal, especially in necrotic pulps (Table V), these streptococci can be considered as possible pathogens. The fact that nonhemolytic streptococci seem to act as possible pathogens might be of importance from the point of view of focal infection and endocarditis.

The D streptococci persist tenaciously in root canals, as can be seen from their higher frequency in later cultures (Table III), from the high ratio of organisms per canal (Table I), and from the long series of consecutive cultures from one canal (Table V). *Streptococcus liquefaciens* is even more persistent in this respect than *Streptococcus faecalis*. D streptococci are difficult to eliminate from the root canal.

This persistence seems to point to a possible role as a pathogen. One would then expect a higher frequency in cultures from infected pulps than from vital pulps. The observed difference, however, is negligible (Fig. 4) or absent (Fig. 3). It should be remembered that the frequency of chance contaminants (for example, micrococci and diphtheroids) is definitely lower in cultures from necrotic pulps (Fig. 4). The D streptococci take an intermediate position between the chance contaminants which occur less frequently in cultures from necrotic pulps and the organisms which are considered possible pathogens because they are more frequent in cultures from necrotic pulps. We think that the expected higher frequency of D streptococci in cultures from necrotic pulp is obscured by the large chance of contamination by this organism. The high frequency of the number of series of consecutive positive cultures of D streptococci from necrotic pulps (68 per cent) compared with the frequency from vital pulps (45 per cent, Table V) supports the view that D streptococci are possible pathogens.

These results seem to point to a large chance of contamination with D streptococci. In some cases they seem to be able to cause clinical infections, and if they do they are difficult to eliminate. For these reasons, we think that they should be considered potential pathogens.

Lactobacilli seem also to be more frequent in necrotic pulps and are occasionally able to persist (Table V). Without further data, no conclusion is warranted since the numbers are too small.

SUMMARY

The bacteriologic results from more than 4,000 root canal cultures are discussed. Streptococci form 61 per cent of the isolated organisms. Among these

the group of hemolytic, indifferent, and indifferent anaerobic streptococci, mainly belonging to serologic groups F, G, and C, seem the most serious possible pathogens. D streptococci (especially *Streptococcus liquefaciens*) are difficult to eliminate from the root canal and are also potential pathogens. *Streptococcus mitis* seems of much less importance, and all other organisms are to be considered as chance contaminants.

Many persons from the staff of the Laboratory have helped with the isolation and identification of organisms or with the calculation of results. Special thanks are due Mr. R. Brinkenburg v. Backum, Mr. H. Ottens, Miss H. G. S. Vreede, Miss W. I. A. v. Thienen, and Miss M. H. G. Tressel.

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Section by the

ARMED FORCES AND PUBLIC HEALTH SERVICE

THE EFFECTS OF VARIOUS LEVELS OF SWEET PEAS (LATHYRUS ODORATUS) IN THE DIET, WITH PROTEIN AND AMINO ACID SUPPLEMENTATION, ON THE ALVEOLAR BONE OF YOUNG RATS

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INTRODUCTION

DESPITE the well-known and striking effects of sweet-pea diets on skeletal growth and ossification, relatively few data are available concerning a possible relationship of experimental lathyrism and oral pathology. The effects of *Lathyrus odoratus* diets upon the alveolar bone of weanling rats have been initially described as diminished alveolar bone and reduced number of trabeculae in the supporting bone of rats fed nonsupplemented 50 per cent sweet-pea diets.[1]

The present report deals with the alveolar bone of animals fed nonsupplemented 30 per cent sweet-pea diets in addition to protein- and amino-acid-supplemented 30 per cent sweet-pea diets. The purpose of this study was to investigate the effects of various levels of dietary protein and amino acids on skeletal growth as it applies to the alveolar process of the mandible and the maxilla. Pair-fed controls were used to evaluate the influence of protein supplementation on the changes observed by feeding the lathyrus diets.

EXPERIMENTAL MATERIALS AND METHODS

Ninety-six male albino weanling rats, each weighing 45 to 50 grams, of the Holtzmann-Sprague-Dawley strain were used throughout this investigation. The rats were divided into groups at weaning and placed on various diets containing sweet peas. An additional group of male rats were pair fed and served as normal littermate controls.

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Diets.—The experimental diet was as follows: *Lathyrus odoratus* meal, 50 per cent; casein, 10 per cent; cornstarch, 25 per cent; sucrose, 5 per cent; brewers' yeast powder (dried), 4 per cent; salt mixture (Hubbell and associates[2]), 4 per cent; cod-liver oil, 2 per cent. The experimental nonsupplemented 50 per cent sweet-pea diets were given for one, two, and three weeks, respectively (S.P. I, S.P. II, S.P. III).

The control diet contained the same ingredients as the experimental diet, but the *Lathyrus odoratus* meal was replaced by a 50 per cent dried and ground commercial edible pea meal.

The protective diets (*Lathyrus odoratus* 30 per cent, plus dietary supplements) were as follows:

P.D. I:* This was a control diet for all protective groups, no supplements being added. It consisted of ground sweet peas, 30 per cent; casein, 10 per cent; starch, 45 per cent; sucrose, 5 per cent; brewers' yeast, 4 per cent; salt mixture,[2] 4 per cent; and cod-liver oil, 2 per cent.

The following are experimental diets plus supplements:

P.D. II: Ground sweet peas, 30 per cent; casein, 40 per cent; starch, 15 per cent; sucrose, 5 per cent; brewers' yeast, 4 per cent; salt mixture,[2] 4 per cent; and cod-liver oil, 2 per cent.

P.D. III: Ground sweet peas, 30 per cent; gelatin, 25 per cent; sucrose, 5 per cent; starch, 30 per cent; brewers' yeast, 4 per cent; salt mixture,[2] 4 per cent; and cod-liver oil, 2 per cent.

P.D. IV: Ground sweet peas, 30 per cent; casein, 35 per cent; glutamine, 5 per cent; cysteine hydrochloride, 4 per cent; sucrose, 5 per cent; starch, 11 per cent; brewers' yeast, 4 per cent; salt mixture,[2] 4 per cent; and cod-liver oil, 2 per cent.

P.D. V: Ground sweet peas, 30 per cent; casein, 10 per cent; glutamine, 5 per cent; sucrose, 5 per cent; cysteine hydrochloride, 4 per cent; starch, 36 per cent; brewers' yeast, 4 per cent; salt mixture,[2] 4 per cent; and cod-liver oil, 2 per cent.

P.D. VI: Ground sweet peas, 30 per cent; casein, 10 per cent; sucrose, 5 per cent; cysteine hydrochloride, 4 per cent; starch, 41 per cent; brewers' yeast, 4 per cent; salt mixture,[2] 4 per cent; and cod-liver oil, 2 per cent.

*P.D. is used as an abbreviation for protective diets.

P.D. VII: Ground sweet peas, 30 per cent; casein, 10 per cent; glutamine, 5 per cent; starch, 40 per cent; sucrose, 5 per cent; brewers' yeast, 4 per cent; salt mixture,[2] 4 per cent; and cod-liver oil, 2 per cent.

Protein-supplemented 30 per cent lathyrus diets (P.D.) were given for eight weeks.

FINDINGS

Alveolar Bone (Protective Diets).—The response to lathyrism was noted to be marked in bone tissue.

The effects of experimental sweet-pea feeding in the rats fed protective diet I without dietary supplements may be described as a diminution of alveolar bone formation, a reduction in the number of trabeculae in the supporting bone, and root and alveolar bone resorption (Fig. 1). The alveolar bone had lost its character of an uninterrupted lamina dura (bundle bone), showing an alteration in the resorption-apposition pattern with lack of apposition on the distal surface of the interdental septum. The physiologic process of resorption was greatly disturbed on the mesial surface of the interdental septum; therefore, the normal or physiologic distal drift of the molars had ceased.

Both mesial and distal surfaces of the interdental septum showed modeling activities consisting mainly of vacuolization or Howship's lacunae indicating resorption with a few isolated osteoblasts arranged beadlike along the distal surface of the interdental septum and at the alveolar crest.

The supporting alveolar bone exhibited a loss of density with decreased trabeculations and an increase in the size of the marrow cavities (Fig. 3). The large amount of marrow tissue was of the hematopoietic type (Fig. 5). One of the most severely affected areas of the jaws was the alveolar bone of the bifurcations. There was considerable fibrous displacement of the marrow tissue in the gingival and basal halves of the alveolar septum.

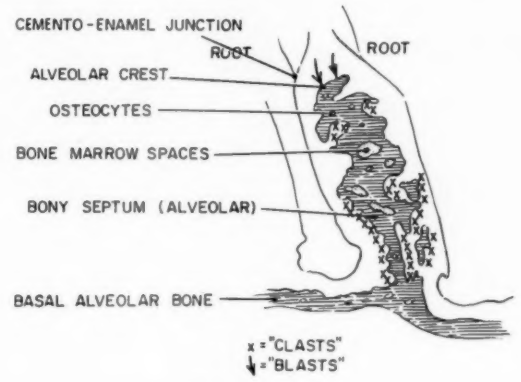
Resorption and osteoclastic activity were generally prominent in the alveolar septum, where many osteoclasts were seen in the interradicular endosteum. The pronounced resorption gave the impression of an acute tissue breakdown, with no attempts at replacement. The level of the alveolar crest advanced occlusally to the same level as the cementoenamel junction by a continued but minimal apposition of bone at the alveolar crest. Osteoid borders were slight along the alveolar septum.

The third molar impinged on the alveolar bone in some areas of the bifurcation. The alveolar bone was seen to be stained more or less densely with hematoxylin, and with this stain it could be recognized as more or less normally calcified bone.

In the group of rats fed protective diet II with protein supplementation, the distance from the cementoenamel junction to the alveolar crest had increased greatly in comparison to protective diet I. The alveolar bone was normal in distribution, character, and number of trabeculations. The bone

marrow was of the hematopoietic type, and the marrow spaces were approximately normal in size (Fig. 2). Resorption and osteoclastic activities were not prominent (Fig. 4). The only resorption present was on the mesial surface of the interdental septum which, together with apposition of bone on the distal surface of this septum, indicated a physiologic distal drift. An osteoid border

Fig. 1.



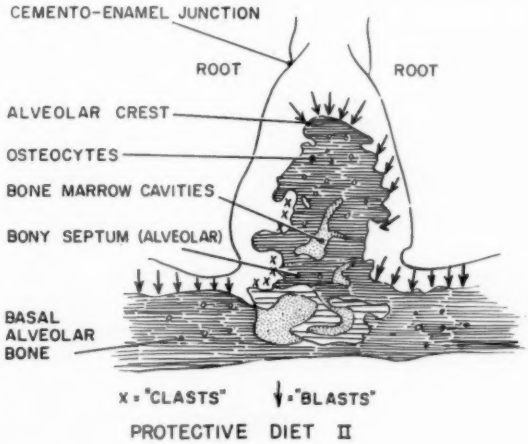


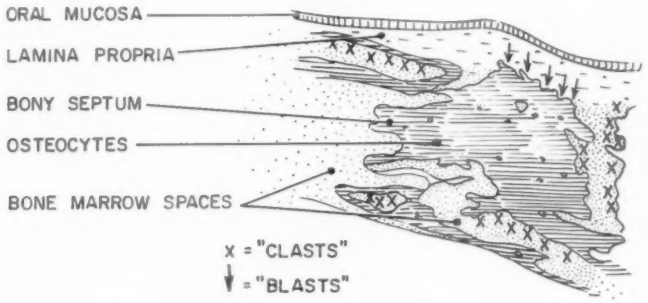
Fig. 2.

Fig. 1.—Camera lucida drawing of the interdental alveolar septum between the upper first and second molars of a male rat fed a 30 per cent nonsupplemented sweet-pea diet for eight weeks. Note the atrophic septum showing a diminished mesiodistal width, the severe osteoclastic activity on both mesial and distal alveolar walls at the basal half of the septum, and the thin basal alveolar bone. (Magnification, ×10; reduced ⅓.)

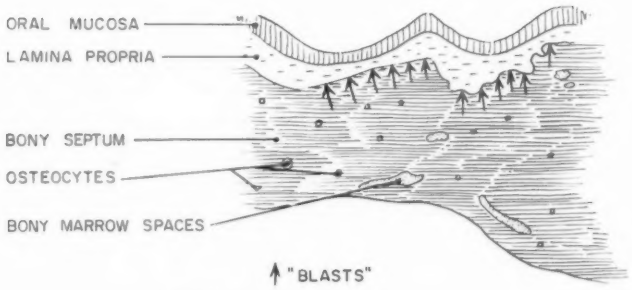
Fig. 2.—Camera lucida drawing of the interdental alveolar septum between the upper first and second molars of a male rat fed a 30 per cent supplemented sweet-pea diet (P.D. II) for eight weeks. This drawing is more or less representative of the alveolar septa of P.D. III, IV, V, VI, and VII groups. Note the wide septum in a mesiodistal dimension; the apposition at the alveolar crest, on the distal alveolar wall, and on the basal alveolar bone; the resorption on the mesial alveolar wall; and small marrow spaces. (Magnification, ×10; reduced ⅓.)

was absent on both the periosteal and the endosteal surfaces of the interradicular and interdental alveolar septa. The alveolar septum stained rather intensively with hematoxylin and eosin. Osteoporosis of the interradicular and interdental alveolar septa, which was so prominent in the nonsupplemented protective diet group I, was absent in the majority or minimally present in very few animals (Fig. 6).

Fig. 3.



PROTECTIVE DIET I



PROTECTIVE DIET II

Fig. 4.

Fig. 3.—Camera lucida drawing of the supporting alveolar bone mesial to the upper first molar of a male rat fed a nonsupplemented sweet-pea diet for eight weeks. Note the increase in osteoclastic activity on both the endosteal and the periosteal surfaces. The marrow spaces have greatly increased in size and contain loose connective tissue (osteoporosis). Magnification, ×10; reduced ⅓.)

Fig. 4.—Camera lucida drawing of the supporting alveolar bone mesial to the first molar of a male rat fed a supplemented sweet-pea diet for eight weeks (P.D. II). This drawing is also more or less representative of the supporting bone of P.D. III, IV, V, VI, and VII groups. Note the wide bony septum with numerous osteoblasts along the surface of the bone. Resorption is absent and bone marrow spaces are very small (no osteoporosis). Magnification, ×10; reduced ⅓.)

Fig. 5.—Photomicrograph of the interdental alveolar septum between the upper first and second molars of a male rat fed at 30 per cent nonsupplemented sweet-pea diet for eight weeks (P.D. I). Note the increase and enlargement of marrow spaces in the gingival half of the septum. The basal half of the septum shows a tremendously enlarged central marrow cavity with connective tissue infiltrating into the bundle bone (osteoporosis). (Hematoxylin and eosin stain. Magnification, ×100; reduced ⅝.)

Fig. 6.—Photomicrograph of the interdental alveolar septum between the upper first and second molars of a male rat fed a 30 per cent supplemented sweet-pea diet (P.D. II) for eight weeks. Note the broad, well-calcified trabeculae of the gingival half of the septum. Endosteal osteoclastic activity is not present (no osteoporosis). (Mallory's phosphotungstic acid-hematoxylin stain. Magnification, ×100; reduced ⅝.)

Fig. 5.

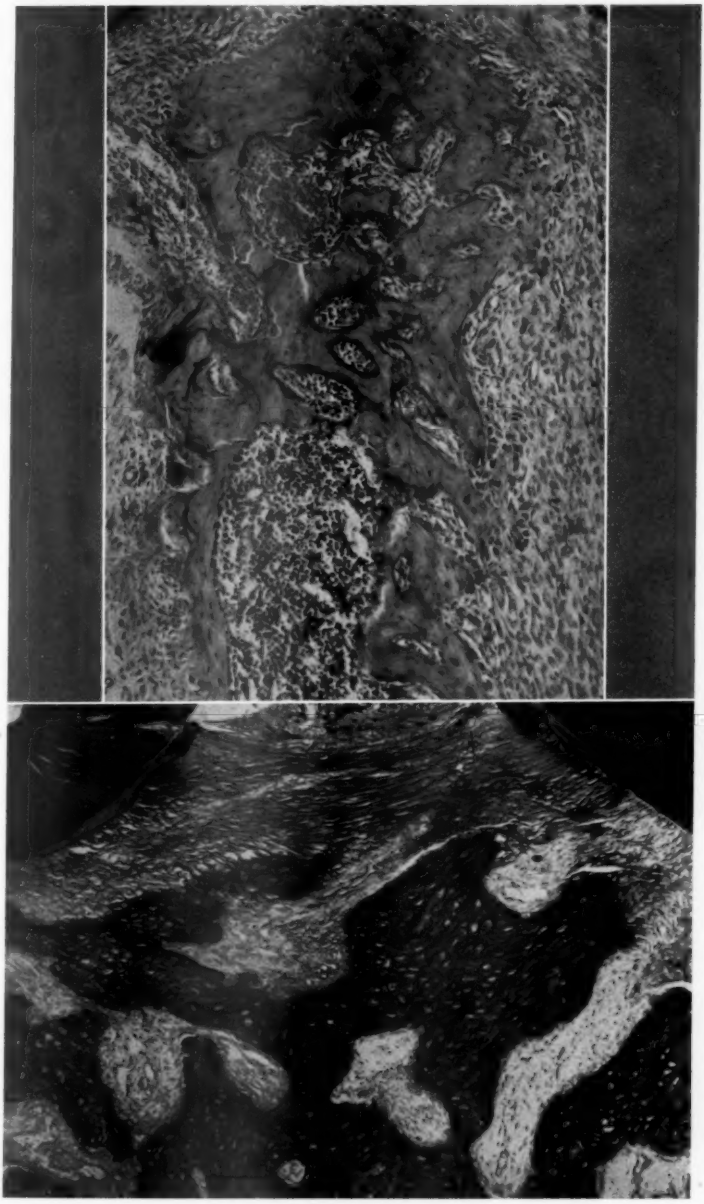


Fig. 6.

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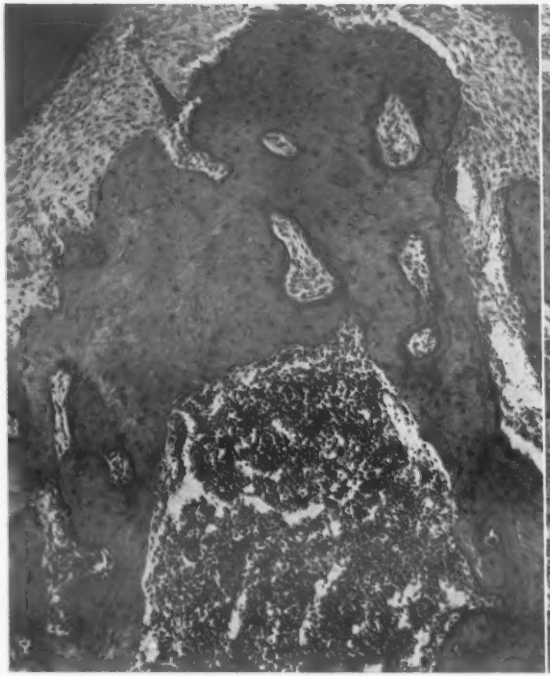

Fig. 7.

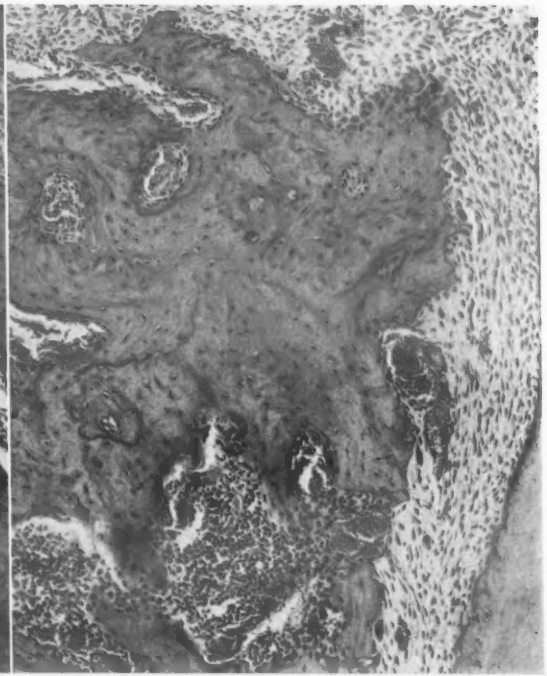

Fig. 8.

Fig. 7.—Photomicrograph of the interdental alveolar septum between the upper first and second molars of a male rat fed a 30 per cent supplemented sweet-pea diet (P.D. III) for eight weeks. Note the small marrow spaces in the gingival half of the septum with wide zone of bundle bone and one large basal marrow cavity. Endosteal and periosteal resorption is absent (no osteoporosis). Apposition is occurring at alveolar crest. (Hematoxylin and eosin stain. Magnification, ×80; reduced ⅓.)

Fig. 8.—Photomicrograph of the interdental alveolar septum between the upper first and second molars of a male rat fed a 30 per cent supplemented sweet-pea diet (P.D. IV) for eight weeks. Note the broad and well-calcified septum and small marrow spaces in the gingival half of the septum. Apposition is occurring at the alveolar crest. (Hematoxylin and eosin stain. Magnification, ×100; reduced ⅓.)

In the group given protective diet III, the supporting bone was dense and contained marrow cavities of normal size, with slight or no infiltration of the hematopoietic bone marrow tissue (Fig. 7). The distance from the cementoenamel junction to the alveolar crest had also increased in comparison to that seen in animals fed protective diet I. The trabeculations were numerous, and their character and distribution were essentially normal. Osteoid was absent from the periosteal and endosteal surfaces of alveolar bone. The alveolar bone consisted of an almost uninterrupted lamina compacta showing the resorption-apposition pattern indicative of the physiologic distal migration or drift of the molars; the distal surface of the interdental septum was covered with osteoblasts arranged in a row, whereas the mesial surface showed Howship's lacunae, indicating resorption. Osteoclastic activity was absent at other sites in the alveolar septum. The alveolar bone of this group stained intensively with hematoxylin and eosin.

Osteoporosis had not developed in either the interradicular or the interdental alveolar septum. There was a balance in the alveolar bone between the catabolic and anabolic tissue changes due to protein supplementation of the diet, therefore preventing the osteoporosis.

In the group given protective diet IV, the alveolar crest consisted of compact lamellated bone, with osteoblasts lining the distal surface, while resorption lacunae were seen on the mesial surface. Newly formed bone was present with large and plump cells lining the surfaces of new trabeculae indicating that bone formation was taking place at the time of sacrifice. The distance from the cementoenamel junction to the level of the alveolar crest had considerably increased in comparison to the group given the nonsupplemented protective diet I. The trabeculae in the alveolar septum were numerous and prominent. The marrow spaces were not enlarged and were occupied by hematopoietic bone marrow tissue (Fig. 8). Resorption and osteoclastic activity were not prominent on the endosteal and periosteal surfaces of the alveolar septum. Osteoid borders were absent from both endosteal and periosteal surfaces of the alveolar septum.

Calcification appeared normal; the alveolar crest and septum stained intensively with hematoxylin.

In the group of animals given protective diet V, the alveolar crest and septum consisted of compact lamellated bone with active resorption of the mesial surface, while the distal side showed bone apposition. Therefore, with dietary supplementation the alveolar crest and septum were capable of maintaining the resorption-apposition pattern, while little or no apposition takes place in animals fed protective diet I without protein supplementation. The distance from the cementoenamel junction to the alveolar crest had continued to increase due to the rate of eruption exceeding the rate of apposition of bone at the alveolar crest. The physiologic distal drift was occurring in a normal manner. The distribution of bone marrow was normal, and the marrow

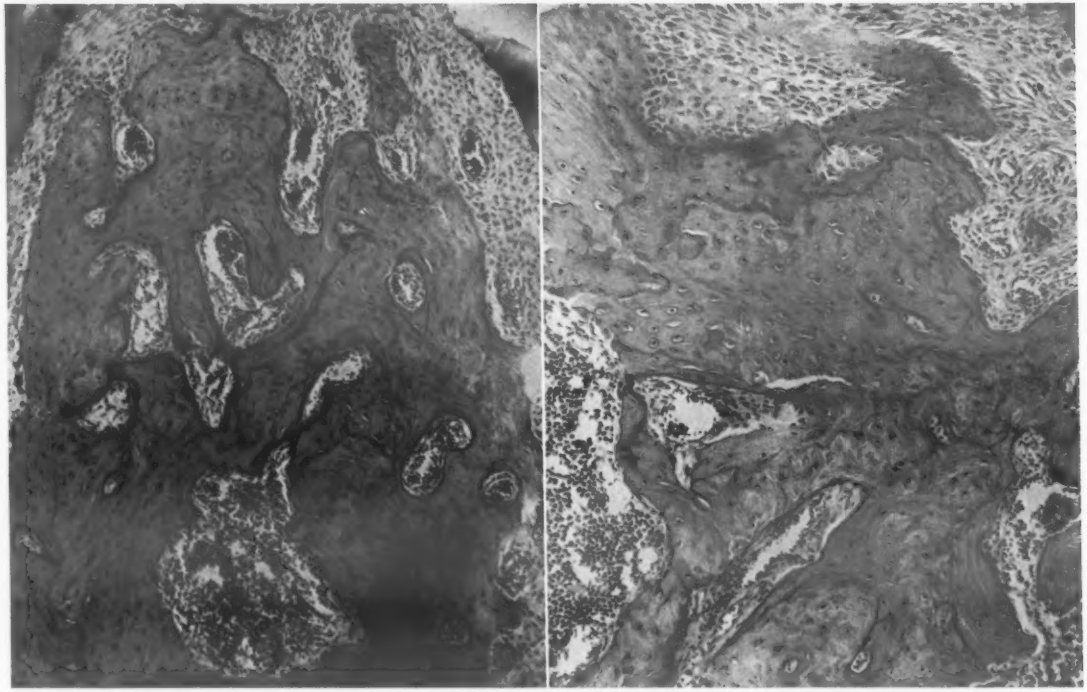

Fig. 9. Fig. 10.

Fig. 9.—Photomicrograph of the interdental alveolar septum between the upper first and second molars of a male rat fed a 30 per cent supplemented sweet-pea diet (P.D. V) for eight weeks. Note the broad gingival half of the septum with marrow cavities and a wide layer of bundle bone. The basal portion contains one large marrow space with an absence of endosteal and periosteal resorption (no osteoporosis). (Hematoxylin and eosin stain. Magnification, ×80; reduced ⅓.)

Fig. 10.—Photomicrograph of the interdental alveolar septum between the upper first and second molars of a male rat fed a 30 per cent supplemented sweet-pea diet (P.D. VI) for eight weeks. Note the apposition (osteoid) of bone at the alveolar crest and small marrow spaces in the gingival third of septum. Septum is well calcified, and osteoclastic activity is absent (no osteoporosis). (Hematoxylin and eosin stain. Magnification, ×100; reduced ⅓.)

appeared to be of the hematopoietic type. Trabeculations of alveolar bone were prominent, as well as normal in amount (Fig. 9). Osteoporosis was absent in both the interradicular and interdental alveolar septa.

In the group given protective diet VI, the alveolar bone consisted of almost uninterrupted bundle bone. The interdental and interradicular septa showed evidence of resorption on the mesial surface, whereas apposition was apparent on the distal surface. The supporting bone contained normal marrow cavities filled with hematopoietic tissue. Resorption and osteoclastic activity were not prominent on either endosteal or periosteal surfaces of bone trabeculae (Fig. 10).

Fig. 11.—Photomicrograph of the interdental alveolar septum between the upper first and second molars of a male rat fed a 30 per cent supplemented sweet-pea diet (P.D. VII) for eight weeks. Note the broad, well-calcified septum mesiodistally with many small marrow spaces in both the gingival and basal halves of the septum. Endosteal and periosteal resorption was absent (no osteoporosis). (Hematoxylin and eosin stain. Magnification, ×100; reduced ⅓.)

Osteoporosis of the interdental and interradicular alveolar septa was minimal, with a few animals of this group showing slight to moderate osteoporosis. The physiologic distal drift was present.

In the group of rats given protective diet VII, the supporting bone was dense, showing a few small marrow cavities. The small amount of marrow

tissue appeared to be of hematopoietic type. The trabeculations were normal in distribution and character. Resorption and osteoclastic activities were not prominent on either the interradicular or the interdental alveolar septa (Fig. 11). Osteoid borders did not occur on the periosteal and endosteal surfaces of bone trabeculae. Calcification appeared normal. The physiologic distal drift was present in all molars, indicating a balanced resorption-apposition pattern.

Alveolar Bone (Sweet-Pea Diets—Nonsupplemented).—The effects of sweet-pea feeding in the rats fed nonsupplemented 30 per cent sweet-pea diets consisted of a progressive diminution of alveolar bone formation together with osteoporosis of the supporting bone. Osteoporosis of the alveolar and supporting bone became accentuated with continued sweet-pea feeding and led finally to pronounced breakdown of bone tissue where an increased rate of resorption occurred.

In the group of rats fed 50 per cent nonsupplemented sweet peas for one week the distance from the alveolar crest to the cementoenamel junction was considerable in the first and second molars, but the third molar was unerrupted. The bone marrow was normal in character and distribution and was of the hematopoietic type. Trabeculations were numerous and normal in appearance. Generally osteoclastic activity was absent, with physiologic resorption only on the distal alveolar wall. Osteoid borders were absent on the endosteal and periosteal surfaces of bone trabeculae. Calcification of alveolar bone was progressing normally.

In the group of rats fed nonsupplemented sweet-pea diet II, the distance from the cementoenamel junction to the alveolar crest failed to increase in comparison with sweet-pea group I. This was apparently due to a decreased rate of eruption and continued apposition of bone at the alveolar crest. There was an increase in the size of the hematopoietic bone marrow spaces in the basal and gingival half of the interradicular and interdental alveolar septa. There was an initial decrease in the trabeculations throughout the alveolar septum. There was an increase in resorption and osteoclastic activity in both the interradicular and interdental alveolar septa. Osteoid borders were absent on the periosteal and endosteal surfaces of bone trabeculae. The alveolar bone stained intensely with hematoxylin. The physiologic distal drift was no longer prominent. The interdental alveolar septum showed evidence of resorption on the mesial surface, whereas no apposition was apparent on the distal surface.

In the group of rats fed nonsupplemented sweet-pea diet III, the interdental alveolar septum showed evidence of resorption on the mesial surface, whereas no apposition was apparent on the distal surface. The supporting bone contained very large marrow cavities with fatty infiltration of the hematopoietic tissue being absent or very minimal. In this group of rats there was pronounced destruction of the alveolar bone. Only a few fragments of bone persisted, and resorptive activities were highly evident with severe osteoporosis of both interradicular and interdental alveolar septa. There was very little supporting bone to maintain the tooth in its normal position, and

fibrous tissue had invaded the enlarged marrow cavities. The most severely affected area of the jaws was the alveolar bone of the bifurcations. The cells lining the surface of the remaining trabeculae were small and flattened, indicating that no bone formation was taking place at the time of sacrifice. The alveolar crest was adjacent to the cementoenamel junction due to the almost complete cessation of eruption and to slight apposition of bone at the height of the alveolar crest. Resorption and osteoclastic activities were very prominent throughout all of the alveolar bone. Osteoid borders were absent generally throughout both the interradicular and interdental alveolar septa.

DISCUSSION

The influence of sweet-pea feeding (beta-aminopropionitrile) on the supporting mineralized tissues of the teeth appears to be part of the generalized tissue response to this toxin.[3-9] The response of alveolar bone, however, may indicate some resemblance to long bone responses. The lathyrus toxin stimulates marked periosteal and endosteal osteoclastic activity in the alveolar bone, thus increasing the size of the marrow spaces. These observations are similar to those made in long bones where, in rat femurs and tibias, endosteal resorption occurred.[7-9]

In this investigation alveolar bone resorption in the molar areas has been observed and can be ascribed to sweet-pea feeding in young growing rats.

Atrophy and wasting-away of alveolar bone tissue are important findings in lathyrism. The fact that the alveolar bone of the bifurcation appears to be the most severely affected may be explained from a functional viewpoint. Very few principal periodontal ligament fibers are normally present here; hence, this parts plays a minor role in supporting the tooth.

It seems appropriate to ask whether the severe osteoporosis seen in sweet-pea-fed animals, without protein supplementations added to their diets, is due entirely to lack of bone apposition or to a combination of this and an increased rate of resorption. Some clarification or insight may be obtained by comparing the nonsupplemented sweet-pea groups with the supplemented protective groups (P.D. II to P.D. VII). The deficiency of casein, gelatin, and the other dietary restrictions, together with the lathyrus toxin present in the nonsupplemented sweet-pea groups and in the protective diet I (nonsupplemented) group, respectively, has caused the inhibition of considerable alveolar bone apposition plus an increased rate of bone resorption with a distinct and severe osteoporosis. Thus, both processes are active during experimental lathyrism.

By comparison, the protein-supplemented diets (P.D. II to P.D. VII) are responsible for normal apposition of alveolar bone with a decreased rate of bone resorption showing an absence of osteoporosis.

It is hypothesized, therefore, that the nonsupplemented sweet-pea diets are responsible for an increased rate of bone resorption, whereas the protein-supplemented protective diets are responsible for an absence of osteoporosis.

Another fact confirming the foregoing hypothesis concerning apposition of bone is that the distance from the alveolar crest to the cementoenamel junction is greater in the supplemented sweet-pea diets (protective diets II to VII) than in either P.D. I or S.P. I, II, and III. This may be attributed to the fact that apposition of alveolar bone is taking place at the alveolar crest; however, the rate of eruption is greater than the rate of apposition of bone at the crest, resulting in an increase in this distance. Thus, the protein-supplemented diets appear to be responsible for continued apposition of bone.

On the basis of the findings utilizing various staining techniques, it is suggested that calcification of remaining alveolar bone was not sufficiently disturbed to reflect any differences between sweet-pea-fed animals with and without the addition of dietary supplements. Thus, lathyrism does not appear to be a disturbance in calcium and phosphorus metabolism; rather, it seems to be a primary disturbance in the metabolism of mesodermal tissues.

The retardation of skeletal growth (that is, alveolar bone) in this study is more severe than but similar to the alveolar bone changes previously reported in rats and mice submitted to deficiencies of the entire vitamin B complex[10] and to deficiences of individual B vitamins (riboflavin,[11, 12] pyridoxine,[13] pantothenic acid,[14, 15] or protein deprivation.[16, 17]).

The changes observed in alveolar bone are more severe than those observed in, for instance, the hypophysectomized rat. No pathologic changes have been reported in the pituitary gland or any other endocrine organ during experimental lathyrism. Therefore, the severity of the changes observed cannot be due primarily to diminished pituitary activity; rather, they are due to interference with the metabolism of the target organ, alveolar bone itself, as a result of the direct action of the lathyrus toxin in the diet. It must be pointed out that such severe bony changes in the alveolar septum were not found in the corresponding pair-fed controls or in the protective groups fed protein supplementation, so that the inanition per se was not a factor in the severity of the changes.

SUMMARY AND CONCLUSIONS

The results of this study demonstrate the striking effects of sweet-pea diets on skeletal growth of the alveolar bone of the rat.

Skeletal alveolar growth was strikingly decreased by *Lathyrus odoratus* intake, because of the beta-aminopropionitrile content of *Lathyrus odoratus* (sweet-pea).[18, 19] Invariably, the animals fed the nonsupplemented lathyrus diet were more severely affected than the corresponding pair-fed controls or the supplemented protective diet groups.

Histologic studies of the alveolar bone revealed the following changes which were always more severe in nonsupplemented than in supplemented lathyrus diets: decrease in the distance from the cementoenamel junction to the alveolar crest; decreased trabeculation of the alveolar bone; increased size of hematopoietic bone marrow spaces; excessive resorption and osteoclastic activity; osteoporosis of interradicular and interdental alveolar septa; and

cessation of the physiologic distal drift of the molars. The most extreme changes were shown by animals on the 50 per cent sweet-pea diet for three weeks and on the 30 per cent sweet-pea diet for eight weeks (P.D. I). All of the protective diets produced varying degrees of improvement in the alveolar bone. The high-casein and high-gelatin diets caused the greatest improvement in alveolar bone growth as well as in decreased osteoclastic activity.

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IDENTICAL BILATERAL ORAL CARCINOMA

*Theodore A. Lesney, Captain (DC) USN**

THIS is a report of an unusual distribution of carcinoma in the oral tissues. It is unusual in that the lesions were similar in onset, course, and duration and remarkably similar in anatomic location, although they occurred on opposite sides of the mouth.

The lesions were microscopically proved to be squamous-cell carcinoma and were the primary focus of this disease. There was a progressive spread by extension of both lesions, but other metastasis, as through lymphatic channels, could not be ascertained. A thorough systemic review revealed no other evidence of cancer.

The two identical oral lesions occurred at about the same time. They were found at (and beyond) the posterior periphery of a full lower denture prosthesis. The patient consulted a dentist because of a growth in her mouth that interfered with the fit of her denture. An ulcerated, friable mass of gingival tissue was seen growing over the superomedial aspects of the posterior body of the mandible in the general vicinity of those areas formerly occupied by the lower third molars. The tumorous mass was creeping by extension into the floor of the mouth and, further, into the base of the tongue. The tumors were not only similar in appearance and location but they were also remarkably alike in the manner in which they were spreading.

CASE REPORT

A 59-year-old Caucasian woman of Balkan extraction presented with the chief complaint of "sores in my mouth that keep getting bigger and interfering with the fit of my plate." The present history disclosed that one and one-half years earlier she had first noted two small ulcers at the sites of the present tumors. She believed that these were decubital ulcers, similar to others that she had experienced while her new lower denture was settling into functional position. These two "sores" differed from the others, however, in that they were not painful. For this reason, she procrastinated in seeking advice while she awaited the anticipated healing. The healing did not occur. As a matter of fact, over a period of several months the ulcerated lesions were seen to spread. She then consulted the same dentist who had fabricated the original denture prosthesis, and he reportedly advised the patient not to wear her denture for a period of several weeks. During this period there was some healing of the ulcers, but the elevated masses of gingival growth did not disappear. The patient was then referred to a physician, who

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provided some local medication (no other details available) and advocated that the patient get another, better-fitting lower denture. She went back to her dentist and had a new lower denture fitted and constructed. Within a period of several months thereafter, however, it was necessary to refit and refabricate the entire lower denture. In each instance, the loss of denture adaptation was due primarily to the progressive growth of the gingival tumor mass. After this episode of about one and one-half years' duration, she was referred to this hospital for evaluation.

Examination at this time revealed two ulcerating masses of gingival mucosa, remarkably similar in appearance and in exactly the same anatomic location on opposite sides of the mouth. The lesions were seen under, and extending beyond, the posterior periphery of a loose-fitting lower denture prosthesis. They were about 1 by 2.5 cm. in size and were spreading by continuity to involve the floor of the mouth and the base of the tongue. The tumor masses were friable and inflamed. The surface epithelium was grayish white in appearance.

The past history, other than as stated, and the family history were found to be noncontributory to the present problem.

The patient had no complaints other than those directly related to her oral problem, and a thorough systemic review failed to disclose any associated physical findings. There was no demonstrable evidence of cancer anywhere else in the body.

Under local anesthesia, a subtotal section was taken from each of the bilateral opposing tumors for microscopic evaluation.

The histologic diagnosis for each of the sections submitted was clearly established as squamous-cell carcinoma. Both microscopic examinations revealed invasive epidermoid cancer in varied degrees of anaplasia and differentiation. Frequent mitotic figures were seen throughout the specimens. The floor of the mouth and the base of the tongue were found to be involved by extension from the primary lesions in the gingivae.

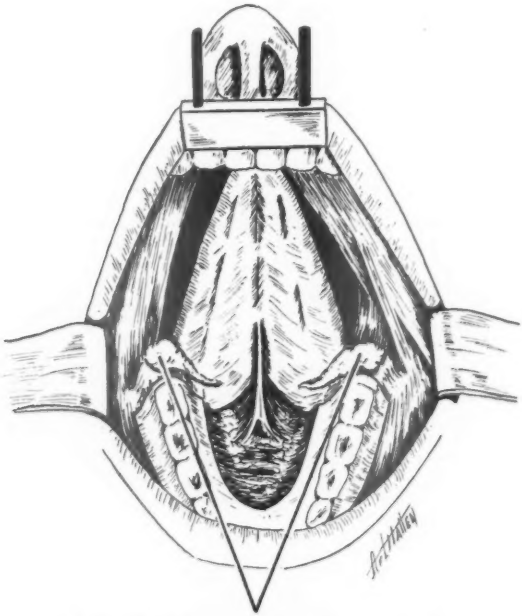
This case was presented and discussed before the Tumor Board. It was recommended that cobalt irradiation therapy be provided, and this was done.

DISCUSSION

The dearth of professional literature concerning identical primary lesions of oral carcinoma, bilaterally and symmetrically dispersed, provoked this case report. Ordinarily, the oncologist may think of oral cancer as a single, primary lesion spreading by continuity or metastasizing via the lymphatics, the blood stream, or both. Two primary tumors of the same histologic origin, remotely spaced as regards location, are indeed a rarity. The question of how far such cancers metastasize beyond demonstrable limits may not be pertinent to this case report, but nevertheless it almost invariably remains unanswered.

The thought arises, of course, that trauma from the lower denture prosthesis may have been in some way related to this disease. Certainly a portion, but not all, of each of these bilateral tumors was located under the denture. While there is no certainty that denture trauma or trauma from any other known source is carcinogenic, the fact remains that persistent trauma to an already existent cancer is most unfavorable. Identical tumors, such as these, in the same areas on opposite sides of the mouth, may support the conjecture that cancer is an all-systemic phenomenon that becomes focused in local areas rather than developing as a local problem and then spreading systemically. However, no conclusions in this regard can be presently founded on fact. Also, the numerous variables in metastasis lend perplexity to the problem. In some cases the rate of spread is slow and seemingly by extension. In others,

there is little or no local spread before lymphatic metastasis is evident. Furthermore, cases of regression and sometimes of complete remission of cancer are occasionally reported. Such limiting factors to the spread of carcinoma, like anatomic barriers and the specific metabolic needs of the tumor, are receiving considerable attention in the current world-wide crash program



IDENTICAL PRIMARY LESIONS
OF ORAL CARCINOMA

Fig. 1.

concerned with the study of cancer. This case may bear some significance if others like it are noted and reported. Otherwise, it may represent only an unusual coincidence, relegated to the category of rarity. Although Kodachrome transparencies and photomicrographs of this particular case are available, their reproduction in black and white for publication resulted in considerable loss of detail. Therefore, a diagrammatic sketch, in lieu of photographs, is provided in Fig. 1.

SUMMARY

A medical rarity—two primary lesions of oral squamous-cell carcinoma, remarkably similar in onset and clinical behavior and located in symmetrical anatomic sites on opposite sides of the mouth—has been presented.

ANNOUNCEMENTS

American Dental Society of Anesthesiology

The sixth annual meeting of the American Dental Society of Anesthesiology will be held at the Hotel Plaza in New York City on Sept. 12 and 13, 1959, just prior to the start of the centennial convention of the American Dental Association.

The general chairman, Dr. Harry M. Seldin, announces that registration for the meeting will begin on Friday, September 11, at 4 P.M. The registration desk will also be open on Saturday, September 12, at 8:30 A.M.

A wide variety of subjects relating to anesthesiology in dentistry will be included in the program, and many well-known personalities in the field of anesthesiology will participate.

There will be a luncheon with anesthesia personalities on Saturday, a banquet-lunch on Sunday, and a dinner-dance and cocktail party on Sunday evening. Members of the A.D.S.A. are urged to write in early for reservations for these occasions. Requests should be sent to Dr. William Rakower, 57 West 57th St., New York 19, New York.

University of Texas Dental Branch

A postgraduate course in crown and bridge prosthesis will be offered Oct. 5 to 9, 1959, by the Department of Crown and Bridge Prosthesis, University of Texas Dental Branch, Houston, Texas. Dr. John F. Johnston, professor of fixed and removable partial dentures at the University of Indiana School of Dentistry, will be the visiting lecturer.

The tuition fee for the course will be $150.00, of which $50.00 must accompany the application; the balance is payable on registration. Applications will not be accepted after Sept. 1, 1959.

American Academy of Oral Pathology

At the thirteenth annual meeting held April 17 to 19, 1959, at the Mayo Auditorium, University of Minnesota, the following slate of officers was elected:

President, Colonel Joseph Bernier

President-Elect, Captain Robert Colby

Vice-President, Commander Henry Scofield

Secretary-Treasurer, Robert J. Gorlin

Editor, Donald Kerr

Council, Victor Halperin
Nelson Large
Irving Meyer
Hamilton B. G. Robinson
William Shafer
Richard Tiecke

American Board of Oral Pathology Examiner, Charles Waldron

New York Institute of Clinical Oral Pathology, Inc.

The eighth Herman L. Reiss Memorial Lecture will be held at the New York Academy of Medicine Building, 2 East 103rd St., New York City, on Monday, Oct. 26, 1959, at 8:30 P.M.

The essayist will be James R. Cameron, professor of oral surgery at the Graduate School of Medicine, University of Pennsylvania, and at Temple University School of Dentistry. His subject will be "Oral Surgery at the Crossroads—Which Direction?"

This will be an open meeting to which members of the dental, medical, and allied professions are cordially invited.

University of Illinois

The Division of Postgraduate Education of the College of Dentistry will offer a concentrated two-week course in oral surgery beginning Oct. 19, 1959. The course will consist of lectures and demonstrations designed to cover all phases of exodontia and oral surgery, including applied pharmacology, anesthesiology, and radiology. It will include treatment of cysts, apicoectomy, mouth preparation for dentures, removal of impactions, and management of fractures.

Further information and applications can be obtained from the Division of Postgraduate Education, University of Illinois, College of Dentistry, 808 South Wood St., Chicago 12, Illinois.

University of Washington

The University of Washington School of Dentistry is offering a twenty-four-month course in oral pathology leading to the degree of Master of Science in Dentistry (M.S.D.) beginning in September, 1960. The course will be under the direction of Leo M. Sreebny, A.B., D.D.S., M.S., Ph.D. Special emphasis will be given to training in research in addition to the offering of a sound background in clinical oral pathology. The submission of a satisfactory thesis reporting on research performed will be a partial requirement. More definite information is available in the *Graduate School Bulletin.*

All communications should be addressed to Saul Schluger, D.D.S., Director, Graduate Dental Education, University of Washington, School of Dentistry, Seattle 5, Washington.

REVIEWS OF THE LITERATURE

BOOK REVIEWS

Dental-Medical Emergencies and Complications. Ira Jay Berlove, D.D.S., M.D. Chicago, 1959. Year Book Publishers, Inc. 380 pages. Price, $7.50.

This volume is made up of five parts:

I. General Considerations of Emergency Management
II. Anesthesia
III. Emergency Considerations of Surgery
IV. Hemorrhage
V. Medical Complications in Dental Office

The book serves its purpose in alerting the practitioner in the diagnosis and treatment of emergencies that occur during surgery in the dental office. Case reports are presented throughout the text to illustrate a point. It is recommended as a reference book and should serve as a valuable aid should an emergency occur.

T. J. Cook.

Oral Histopathology. M. A. Rushton and B. E. D. Cooke, University of London. Baltimore, 1959, Williams & Wilkins Company. 190 pages. Price, $7.00.

This text includes chapters on the teeth and their formative elements, the periodontal tissues, the oral mucosa, and the mandible and maxilla.

The illustrations, 214 in number, are excellent. The book is a limited factual presentation which should assist the student and practitioner to understand the nature of changes in the tissues they observe and treat.

T. J. Cook.

ABSTRACTS OF CURRENT LITERATURE

A Limited Survey of Radiation Exposure From Dental X-ray Units. R. O. Gorson, B. S. Halveorsen, M. S. Leebman, and E. V. Aitken: Radiology **72:** 1, January, 1959.

This team of investigators made measurements from fifty-six dental x-ray units, of which forty-two were in the offices of dentists. All calibrations and radiation surveys were performed under normal operating conditions.

They conclude: "The radiation exposure to the dentists and their assistants included in this report appears to be on the average considerably less than 100 mr. per week, the maximum permissible average weekly dose to the total body for occupational exposure as recommended by the National Committee on Radiation Protection. However, the fact that many dentists can receive low radiation exposure in the course of their work indicates that for others there is considerable room for improvement."

T. J. C.

Osteomyelitis of the Mandible Following Irradiation. N. G. Elmer, F. W. Chambers, H. S. Ogden, G. C. Coggs, and J. T. Crave: Radiology **72**: 68, January, 1959.

This experimental study in which the mandibles of dogs were exposed to irradiation by x-ray was made in an effort to determine the effects.

In the first experiment teeth were not removed. The total amount of irradiation delivered ranged from 3,000 to 8,000 r (air) in 1,000 r increments. The animals receiving 5,000 r or more had a severe reaction with the loosening of the teeth. In the second experiment teeth were removed sixteen days prior to irradiation.

The thought is expressed that "removal of teeth prior to irradiation of the mandible significantly decreased the incidence of osteomyelitis."

T. J. C.

Carbon-Black Carcinoma of Stensen's Duct. B. Maisel, C. Pearce, J. Connolly, and J. Pearce: A. M. A. Arch. Surg. **78**: 161/331, February, 1959.

A case is reported in which a 53-year-old white man had a painful nodule in the soft tissues of the right cheek. The family physician believed that there was a stone in Stensen's duct. The nodule was surgically removed and no stone was found. A frozen section was done, and the diagnosis of epidermoid carcinoma, grade 2 or 3, was made.

The patient was a research chemist who experimented in the production of many types of carbon-black. The theory is expressed that the fine particles of carbon-black could proceed through Stensen's duct to the parotid gland. The probable relationship of carbon-black to cancer is discussed.

T. J. C.

Study of Narcotics and Sedatives for Use in Preanesthetic Medication. J. E. Eckenhoff, and M. Helrich: J. A. M. A. **167**: 415, May, 1958.

A study was made to compare the effectiveness of morphine, meperidine, and secobarbital for preanesthetic sedation. The drugs were used in 1,400 patients.

Secobarbital was found to leave the patient calm, carefree, and alert. The narcotics produced a more drowsy or sleepy patient. Cough and laryngospasm were the common complications when thiopental was injected and secobarbital was the preanesthetic sedation.

Routine use of preanesthetic narcotic medication is not advised. Preoperative medication should be ordered to meet the needs of each operative case.

T. J. C.

Thrush Complicating Radiotherapy of the Mouth and Neck. H. H. Eelkema, P. W. Scanlon, M. Y. Colby, Jr., and J. A. Ulrich: Radiology **72**: 26, January, 1959.

Thrush, or moniliasis, is a disease which may be manifested in the oral mucosa in patients with malignant lesions of the head and neck treated by irradiation therapy.

The damage to the mucous membranes of the mouth plus the debilitated condition of the occasional patient treated with roentgen rays is a factor in the occurrence of thrush.

Cultures were made of mucous membrane lesions of the oral cavity in seven patients receiving roentgen or cobalt-60 therapy for malignancy of the head and neck. All cultures were positive for *Candida albicans*.

Nystatin was the drug of choice in the treatment of oral thrush. The oral suspension (Mycostatin, 100,000 units in 1 c.c.) was held in the mouth as long as possible and repeated four times daily.

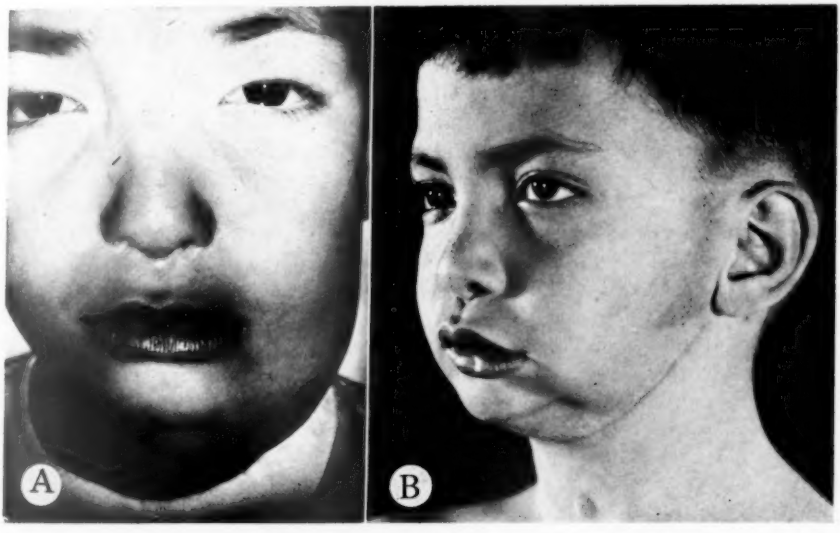
T. J. C.

Neurofibrosarcomas of Cranial Nerve Origin. S. G. Economon, H. W. Southwick, and D. P. Slaughter. A. M. A. Arch. Surg. 77: 271, August, 1958.

Although neurofibrosarcomas of the head and neck are uncommon, when they do occur the difficulties encountered in their diagnosis and care are great.

Fourteen cases are reported; one is cited here.

"Case II.—A 6-year-old boy. The parents of the patient stated that after a fall and injury to the left jaw, three months previously, a swelling appeared in this area. Several weeks after the onset of the swelling he was taken to a dental clinic, where a molar tooth was extracted, with no regression in size of the submandibular mass. A month after the accident the family physician performed a biopsy of this mass, and the microscopic diagnosis was 'chronic inflammation.' The mass contineud to enlarge until he was first seen, in August, 1954.



Preoperative (*A*) and postoperative (*B*) photographs of a patient with a neurofibrosarcoma of the left submaxillary triangle. An en bloc excision of the left hemimandible, contents of the submaxillary triangle, and the left floor of the mouth was performed. The functional and cosmetic results have been satisfactory. (From Economon, Southwick, and Slaughter: *A. M. A. Arch. Surg.*, August, 1958.)

"Physical examination revealed an obvious left submandibular swelling, which was moderately firm, painless, and fixed to the left mandible. There was mild bulging of the floor of the mouth, and the tumor extended slightly to the right of the midline. All the cranial nerves functioned normally. Stereoscopic x-rays of the left hemimandible showed bone destruction along the inferior margin, presumably secondary to invasion by a malignant process. The remainder of the physical examination and all other tests were normal.

"In September, 1954, surgery was performed through a submandibular incision, and full-thickness skin flaps were mobilized, with preservation of the platysma muscle and the mandibular branch of the facial nerve. Biopsy of the tumor was performed, and a frozen section revealed a malignant spindle-cell tumor. The mandible was disarticulated

and also divided at the symphysis menti, and an en bloc excision of the contents of the submaxillary triangle performed. The postoperative convalescence was satisfactory. Since surgery the patient's phonation and chewing ability have been adequate. He is in the process of having a dental prosthesis constructed for better facial symmetry. The final diagnosis was low-grade neurofibrosarcoma. There has been no recurrent disease."

This article is well worth the time it takes to read it.

T. J. C.